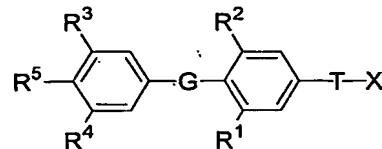


We Claim:

1. A compound of Formula I:

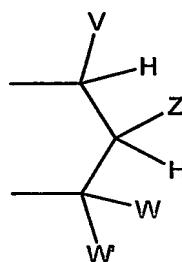


wherein:

- 5      G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,  
-CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C₁-C₄ alkyl)-;
- T is selected from the group consisting of -(CR<sup>a</sup>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup>)<sub>n</sub>-,  
-(CR<sup>a</sup>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup>)<sub>n</sub>-, -O(CR<sup>b</sup>)<sub>n</sub>-(CR<sup>a</sup>)<sub>n</sub>-,  
-S(CR<sup>b</sup>)<sub>n</sub>-(CR<sup>a</sup>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup>)<sub>n</sub>-(CR<sup>a</sup>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup>)<sub>n</sub>-,  
-(CR<sup>a</sup>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup>)<sub>m</sub>-, -(CR<sup>a</sup>)<sub>m</sub>C(O)-, -(CR<sup>a</sup>)<sub>n</sub>C(O)(CR<sup>a</sup>)<sub>n</sub>-,  
-(CR<sup>a</sup>)<sub>n</sub>C(O)(CR<sup>a</sup>)<sub>p</sub>-;
- 10     k is an integer from 0-4;
- m is an integer from 0-3;
- n is an integer from 0-2;
- 15     p is an integer from 0-1;
- Each R<sup>a</sup> is independently selected from the group consisting of hydrogen,  
optionally substituted -C₁-C₄ alkyl, halogen, -OH, optionally substituted -O-C₁-C₄  
alkyl, -OCF<sub>3</sub>, optionally substituted -S-C₁-C₄ alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally  
substituted -C₂-C₄ alkenyl, and optionally substituted -C₂-C₄ alkynyl; with the proviso  
20     that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached  
to the same C is a hydrogen, or attached via a carbon atom;
- Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and  
optionally substituted -C₁-C₄ alkyl;
- Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and  
25     optionally substituted -C₁-C₄ alkyl, optionally substituted -C(O)-C₁-C₄ alkyl,  
and -C(O)H;
- R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen,  
optionally substituted -C₁-C₄ alkyl, optionally substituted -S-C₁-C₃ alkyl, optionally  
substituted -C₂-C₄ alkenyl, optionally substituted -C₂-C₄ alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally  
30     substituted-O-C₁-C₃ alkyl, and cyano;

- R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>cycloalkyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;
- Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;
- Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;
- R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup> and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;
- Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;
- R<sup>5</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);
- X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;
- Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from

- the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>,
- 5 -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy;
- when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>,
- 10 and -cycloalkylene-COOR<sup>y</sup>;
- when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>,
- 15 -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;
- 20 or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



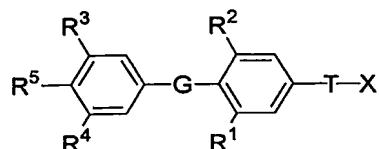
wherein:

- 25 V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- 5        or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;
- 10      or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;
- 15      or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- 20      or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- 25      Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;
- 25      q is an integer 2 or 3;
- 25      Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;
- 25      Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;
- 30      Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;
- 30      Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;
- 30      with the provisos that:

- a) when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each bromo, R<sup>3</sup> is *iso*-propyl, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH, then X is not P(O)(OH)<sub>2</sub> or P(O)(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>;
- b) V, Z, W, W' are not all -H; and
- c) when Z is -R<sup>2</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;
- 5 or pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

2. A compound of Formula I:



- 10 wherein:
- G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;
- T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-,
- 15 k is an integer from 0-4;
- m is an integer from 0-3;
- 20 n is an integer from 0-2;
- p is an integer from 0-1;
- Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;
- 25 Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

Each R<sup>c</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, 5 optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;

R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally 10 substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>cycloalkyl, optionally substituted (CR<sup>a</sup>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;

15 Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;

Each R<sup>e</sup> is optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> 20 alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup>)<sub>n</sub>heterocycloalkyl;

R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally 25 substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup> and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the 30 group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl,

optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

$R^5$  is selected from the group consisting of -OH, optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ , -F,  $-NHC(O)R^e$ ,  $-NHS(=O)R^e$ ,  $-NHS(=O)_2R^e$ ,

5  $-NHC(=S)NH(R^b)$ , and  $-NHC(O)NH(R^h)$ ;

$X$  is  $P(O)YR^{11}Y'R^{11}$ ;

Y and Y' are each independently selected from the group consisting of -O-, and  $-NR^v-$ ; when Y and Y' are -O-,  $R^{11}$  attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted  $CH_2$ -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,

10  $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

15 when Y and Y' are  $-NR^v-$ , then  $R^{11}$  attached to  $-NR^v-$  is independently selected from the group consisting

of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;

when Y is -O- and Y' is  $NR^v$ , then  $R^{11}$  attached to -O- is independently selected

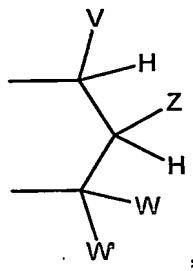
20 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted  $CH_2$ -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,

25  $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and  $R^{11}$  attached to  $-NR^v-$  is independently selected from the group consisting of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from -O- and  $-NR^v-$ , then together

$R^{11}$  and  $R^{11}$  are -alkyl-S-S-alkyl- to form a cyclic group, or together  $R^{11}$  and  $R^{11}$  are the

30 group:



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, 5 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, 10 alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the 15 phosphorus;
- or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that 20 is three atoms from a Y attached to the phosphorus;
- or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- or together W and W' are connected via an additional 2-5 atoms to form a cyclic 25 group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,

- SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
 -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;
- q is an integer 2 or 3;
- 5        Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;  
 Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and  
 aralkyl;
- Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or  
 together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;
- 10      Each R<sup>y</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl,  
 alkoxy carbonyloxyalkyl, and lower acyl;
- with the provisos that:
- a)        when G is -O-, T is -(CH<sub>2</sub>)<sub>0-4</sub>-, R<sup>1</sup> and R<sup>2</sup> are independently halogen, alkyl  
 of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or  
 15      cycloalkyl of 3 to 7 carbons, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH, then X is not -P(O)(OH)<sub>2</sub>  
 or -P(O)(O-lower alkyl)<sub>2</sub>;
- b)        when G is -O-, R<sup>5</sup> is -NHC(O)R<sup>e</sup>, -NHS(=O)<sub>1-2</sub>R<sup>e</sup>, -NHC(S)NH(R<sup>h</sup>),  
 or -NHC(O)NH(R<sup>h</sup>), T is -(CH<sub>2</sub>)<sub>m</sub>-, -CH=CH-, -O(CH<sub>2</sub>)<sub>1-2</sub>-, or -NH(CH<sub>2</sub>)<sub>1-2</sub>-, then X is  
 not -P(O)(OH)<sub>2</sub> or -P(O)(OH)NH<sub>2</sub>;
- 20      c)        V, Z, W, W' are not all -H; and  
 d)        when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl,  
 or heterocycloalkyl;
- and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically  
 acceptable salts of said prodrugs.
- 25      3.        The compound of claim 1 wherein when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup>  
 are each bromo, R<sup>3</sup> is *iso*-propyl, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.
4.        The compound of claim 2 wherein when G is -O-, T is -(CH<sub>2</sub>)<sub>0-4</sub>-, R<sup>1</sup> and  
 R<sup>2</sup> are independently selected from the group consisting of halogen, alkyl of 1 to 3  
 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3  
 30      to 7 carbons, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen; and wherein when G is -O-, R<sup>5</sup> is  
 selected from the group consisting of NHC(O)R<sup>e</sup>, -NHS(=O)<sub>1-2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>),  
 and -NHC(O)NH(R<sup>h</sup>), T is selected from the group consisting  
 of -(CH<sub>2</sub>)<sub>m</sub>-, -CH=CH-, -O(CH<sub>2</sub>)<sub>1-2</sub>-, and -NH(CH<sub>2</sub>)<sub>1-2</sub>-, then R<sup>4</sup> is not hydrogen.

5. The compound of claim 1 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-.
6. The compound of claim 2 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-.
- 5 7. The compound of claim 1 wherein T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -NR<sup>b</sup>(CO)-, and -CH<sub>2</sub>CH(NR<sup>c</sup>R<sup>b</sup>)-.
- 10 8. The compound of claim 2 wherein T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -NR<sup>b</sup>(CO)-, and -CH<sub>2</sub>CH(NR<sup>c</sup>R<sup>b</sup>)-.
9. The compound of claim 1 wherein R<sup>1</sup> and R<sup>2</sup> are the same and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.
- 10 10. The compound of claim 2 wherein R<sup>1</sup> and R<sup>2</sup> are the same and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.
- 15 11. The compound of claim 1 wherein R<sup>1</sup> and R<sup>2</sup> are different and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.
12. The compound of claim 2 wherein R<sup>1</sup> and R<sup>2</sup> are different and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.
- 20 13. The compound of claim 1 wherein R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano and CF<sub>3</sub>.
14. The compound of claim 2 wherein R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano, and CF<sub>3</sub>.
15. The compound of claim 1 wherein R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>.
- 25 16. The compound of claim 2 wherein R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>.
17. The compound of claim 1 wherein R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>.
- 30 18. The compound of claim 2 wherein R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>.
19. The compound of claim 1 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>,

-P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>], and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

20. The compound of claim 2 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>], and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

21. The compound of claim 1 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-; T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -NR<sup>b</sup>(CO)-, and -CH<sub>2</sub>CH(NR<sup>c</sup>R<sup>b</sup>)-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano and CF<sub>3</sub>; R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F and -NHC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>; and X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>] and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

22. The compound of claim 21 wherein when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are bromo, R<sup>3</sup> is *iso*-propyl, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.

23. The compound of claim 2 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-; T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -NR<sup>b</sup>(CO)-, and -CH<sub>2</sub>CH(NR<sup>c</sup>R<sup>b</sup>)-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano, and CF<sub>3</sub>; R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F and -NHC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted (CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>; and X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>,

-P(O)[-N(H)CR<sup>2</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>2</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>], and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

24. The compound of claim 23 wherein when G is -O-, T is -(CH<sub>2</sub>)<sub>0-2-</sub>, R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen, halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen; and wherein when G is -O-, R<sup>5</sup> is -NHC(O)R<sup>e</sup>, T is selected from the group consisting of -(CH<sub>2</sub>)<sub>m</sub>-, -O(CH<sub>2</sub>)<sub>1-2</sub>-, -NH(CH<sub>2</sub>)<sub>1-2</sub>-, then R<sup>4</sup> is not hydrogen.

25. The compound of claim 21 wherein T is -CH<sub>2</sub>CH(NH<sub>2</sub>)-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and halogen; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

26. The compound of claim 25 wherein G is -O-; T is -CH<sub>2</sub>CH(NH<sub>2</sub>)-; R<sup>1</sup> and R<sup>2</sup> are each iodo; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is -OH; and R<sup>3</sup> is iodo.

27. The compound of claim 26 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-t-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-i-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

28. The compound of claim 21 wherein T is -N(H)C(O)-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH, and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl,

optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl,

5 4-fluorophenyl, and 4-pyridyl.

29. The compound of claim 28 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each methyl; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is -CH(OH)(4-fluorophenyl).

30. The compound of claim 29 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>,  
 10 -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>,  
 -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxypyhenyl],  
 -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxypyhenyl],  
 and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

31. The compound of claim 21 wherein T is -OCH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH, and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

32. The compound of claim 31 wherein G is -CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each methyl; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

33. The compound of claim 32 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>,  
 -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>,  
 -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxypyhenyl],  
 30 -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxypyhenyl],  
 and -P(O)[-OCH(3-chlorophenyl) CH<sub>2</sub>CH<sub>2</sub>O-].

34. The compound of claim 21 wherein T is -CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from

the group consisting of -OH, and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl,

- 5 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

35. The compound of claim 34 wherein when G is -O-, R<sup>1</sup> and R<sup>2</sup> are each bromo, R<sup>3</sup> is *iso*-propyl, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.

- 10 36. The compound of claim 34 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *i*-propyl.

37. The compound of claim 36 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, 15 -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphe nyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphe nyl], and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

38. The compound of claim 21 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-; T is -CH<sub>2</sub>CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH, and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

39. The compound of claim 38 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

40. The compound of claim 39 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphe nyl],

-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

41. The compound of claim 23 wherein T is -CH<sub>2</sub>CH(NH<sub>2</sub>)-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, 5 and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and halogen; R<sup>5</sup> is selected from the group consisting of -OH, and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, 10 piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

42. The compound of claim 41 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each iodo; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is -OH; and R<sup>3</sup> is iodo.

43. The compound of claim 42 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], 20 and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

44. The compound of claim 23 wherein T is -N(H)C(O)-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH, and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, 25 optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

45. The compound of claim 44 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each methyl; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is -CH(OH)(4-fluorophenyl).

46. The compound of claim 44 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>,

-P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>,  
-P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

5        47.      The compound of claim 23 wherein T is -OCH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH, and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, 10        optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> where R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

15        48.      The compound of claim 47 wherein G is -CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each methyl; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

49.      The compound of claim 47 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>,  
-P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>,  
-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>,  
-P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

50.      The compound of claim 23 wherein T is -CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, 25        optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> where R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 30        4-fluorophenyl, and 4-pyridyl.

51. The compound of claim 50 wherein when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of iodo, bromo, chloro, and methyl, R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 6 carbons, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.

5 52. The compound of claim 50 wherein G is -O-; T is -CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *i*-propyl.

53. The compound of claim 50 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, 10 -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O) OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

54. The compound of claim 23 wherein T is -CH<sub>2</sub>CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and 15 cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 20 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> where R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

25 55. The compound of claim 54 wherein when G is -O-, R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of iodo, bromo, chloro, and methyl; R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 6 carbons; and R<sup>5</sup> is -OH; then R<sup>4</sup> is not hydrogen.

56. The compound of claim 54 wherein G is -O-; T is -CH<sub>2</sub>CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

57. The compound of claim 54 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],

-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

58. The compound as in any of claims 1, 2, 3, 4, 21, 23, 25, 27, 28, 30, 31, 33,  
34, 37, 38, 40, 41, 43, 44, 46, 47, 49, 50, 53, 54, or 57, wherein X is -PO<sub>3</sub>H<sub>2</sub>.

5 59. The compound of claim 32 wherein X is selected from the group  
consisting of -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub> and -P(O)[-OCH<sub>2</sub>OC(O)-*i*-propyl]<sub>2</sub>.

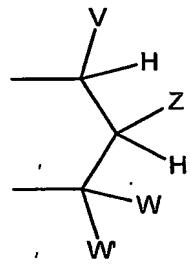
60. The compound of claim 32 wherein X is selected from the group  
consisting of -P(O)[-OCH<sub>2</sub>OC(O)O-ethyl]<sub>2</sub> and -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>.

61. The compound of claim 32 wherein X is selected from the group  
10 consisting of -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>  
and -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>.

62. The compound of claim 32 wherein X is -P(O)[-OCH<sub>2</sub>CH<sub>2</sub>SC(O)Me]<sub>2</sub>.

63. The compound of claim 32 wherein X is selected from the group  
consisting of -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl]  
15 and -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl].

64. The compound of claim 32 wherein X is -P(O)YR<sup>11</sup>Y'R<sup>11</sup>  
wherein Y and Y' are each independently selected from -O- and -NR<sup>V</sup>-; together  
R<sup>11</sup> and R<sup>11</sup> are the group:



20 wherein

V, W, and W' are independently selected from the group consisting of hydrogen,  
optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,  
substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and  
optionally substituted 1-alkynyl;

25 or together V and Z are connected via an additional 3-5 atoms to form a cyclic  
group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining  
atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is

- 5 fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, 10 alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

- 15 or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, 20 -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

with the provisos that:

- 25 a) V, Z, W, W' are not all -H; and  
b) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and 30 aralkyl; and

Each R<sup>y</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl.

65. The compound of claim 64 wherein V is aryl.

66. The compound of claim 65 wherein Z is hydrogen, W is hydrogen, and W' is hydrogen.

67. The compound of claim 66 wherein V is selected from the group consisting of 3-chlorophenyl, 4-chlorophenyl, 3-bromophenyl, 3-fluorophenyl, 5 pyrid-4-yl, pyrid-3-yl and 3,5-dichlorophenyl.

68. The compound of claim 67 wherein the relative stereochemistry between the V-group substituent and T on the dioxaphosphonane ring is *cis*.

69. The compound of claim 68 wherein said *cis* dioxaphosphonane ring has R stereochemistry at the carbon where the V-group is attached.

10 70. The compound of claim 68 wherein said *cis* dioxaphosphonane ring has S stereochemistry at the carbon where the V-group is attached.

71. The compound of claim 19 wherein G is -O-, T is -CH<sub>2</sub>CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each iodo, and R<sup>3</sup> is *iso*-propyl, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH.

15 72. The compound of claim 71 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, and -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

73. The compound of claim 19 wherein G is -O-, T is -CH<sub>2</sub>CH<sub>2</sub>-, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are each iodo, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH.

20 74. The compound of claim 73 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, and -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

25 75. The compound of claim 19 wherein G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each iodo, R<sup>3</sup> is *iso*-propyl, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH.

76. The compound of claim 75 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, and -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

30 77. The compound of claim 19 wherein G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> are each iodo, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH.

78. The compound of claim 77 wherein X is selected from the group consisting of -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>,

and  $-P(O)[-N(H)C(CH_3)_2C(O)OCH_2CH_3]_2$ , and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

79. The compound of claim 19 wherein G is -O-, T is  $-OCH_2-$ , R<sup>1</sup> and R<sup>2</sup> are each iodo, and R<sup>3</sup> is *iso*-propyl, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH.

5 80. The compound of claim 79 wherein X is selected from the group consisting of  $-P(O)[-OCH(V)CH_2CH_2O-]$ ,  $-P(O)[-N(H)CH(CH_3)C(O)OCH_2CH_3]_2$ , and  $-P(O)[-N(H)C(CH_3)_2C(O)OCH_2CH_3]_2$ , and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

10 81. The compound of claim 19 wherein G is -O-, T is  $-CH_2-$ , R<sup>1</sup> and R<sup>2</sup> are each chloro, R<sup>3</sup> is 4-fluorobenzyl, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH.

82. The compound of claim 81 wherein X is selected from the group consisting of  $-P(O)[-OCH(V)CH_2CH_2O-]$ ,  $-P(O)[-N(H)CH(CH_3)C(O)OCH_2CH_3]_2$ , and  $-P(O)[-N(H)C(CH_3)_2C(O)OCH_2CH_3]_2$ , and V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

15 83. A method of preventing or treating a metabolic disease comprising administering to an animal a pharmaceutically effective amount of a phosphonic acid-containing compound, a pharmaceutically acceptable salt thereof, or prodrugs thereof or pharmaceutically acceptable salts of said prodrugs, wherein said phosphonic acid containing compound binds to a thyroid receptor.

20 84. The method of claim 83 wherein said phosphonic acid containing-compound binds to a thyroid receptor with a Ki of  $\leq 1 \mu M$ .

85. The method of claim 84 wherein said thyroid receptor is TR $\alpha$ 1.

86. The method of claim 84 wherein said thyroid receptor is TR $\beta$ 1.

87. The method of claim 84 wherein said phosphonic acid-containing 25 compound binds to a thyroid receptor with a Ki of  $\leq 100 nM$ .

88. The method of claim 87 wherein said thyroid receptor is TR $\alpha$ 1.

89. The method of claim 87 wherein said thyroid receptor is TR $\beta$ 1.

90. The method of claim 83 wherein said metabolic disease is selected from the group consisting of obesity, hypercholesterolemia, hyperlipidemia, atherosclerosis, 30 coronary heart disease, and hypertension.

91. The method of claim 90 wherein said metabolic disease is selected from the group consisting of obesity, hypercholesterolemia, and hyperlipidemia.

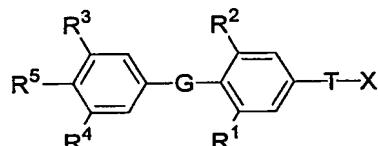
92. The method of claim 83, wherein said phosphonic acid-containing compound activates said thyroid receptor.

93. The method of claim 92 wherein said thyroid receptor is TR $\alpha$ 1.

94. The method of claim 92 wherein said thyroid receptor is TR $\beta$ 1.

5 95. The method of claim 91 wherein said phosphonic acid containing-compound increases mRNA expression of a gene selected from the group consisting of LDL receptor, ACC, FAS, spot-14, CPT-1, CYP7A, apo AI, and mGPDH.

96. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula I:



10

wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-,-CF<sub>2</sub>-,-CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -<sub>15</sub>(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>;

15 k is an integer from 0-4;

20 m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

25 Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;

30 Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, 5 optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;

R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally 10 substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>2</sub>maryl, optionally substituted -(CR<sup>a</sup>)<sub>2</sub>m cycloalkyl, optionally substituted -(CR<sup>a</sup>)<sub>2</sub>m heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;

15 Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub> cycloalkyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub> heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;

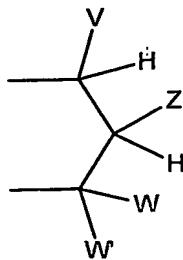
20 Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub> cycloalkyl, and optionally substituted -(CR<sup>a</sup>)<sub>n</sub> heterocycloalkyl;

25 R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub> cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub> heterocycloalkyl, or R<sup>f</sup> and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected 30 from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl,

optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and  
optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

- $R^5$  is selected from the group consisting of -OH, optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ , -F,  $-NHC(O)R^e$ ,  $-NHS(=O)R^e$ ,  $-NHS(=O)_2R^e$ ,  
5  $-NHC(=S)NH(R^h)$ , and  $-NHC(O)NH(R^h)$ ;  
 $X$  is  $P(O)YR^{11}Y'R^{11}$ ;  
 $Y$  and  $Y'$  are each independently selected from the group consisting of -O-,  
and  $-NR^v$ ;- when  $Y$  and  $Y'$  are -O- ,  $R^{11}$  attached to -O- is independently selected from  
the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted  
10 heterocycloalkyl, optionally substituted  $CH_2$ -heterocycloakyl wherein the cyclic moiety  
contains a carbonate or thiocarbonate, optionally  
substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-$   $OC(O)R^y$ ,  
 $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
and -alkyl-S-S-S-alkylhydroxy;  
15 when  $Y$  and  $Y'$  are  $-NR^v$ -, then  $R^{11}$  attached to  $-NR^v$ - is independently selected  
from the group consisting  
of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ ,  
and -cycloalkylene-COOR<sup>y</sup>;  
when  $Y$  is -O- and  $Y'$  is  $NR^v$ , then  $R^{11}$  attached to -O- is independently selected  
20 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted  
heterocycloalkyl, optionally substituted  $CH_2$ -heterocycloakyl wherein the cyclic moiety  
contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  
 $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-$   $OC(O)R^y$ ,  
 $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
25 and -alkyl-S-S-S-alkylhydroxy; and  $R^{11}$  attached to  $-NR^v$ - is independently selected from  
the group consisting of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ ,  
and -cycloalkylene-COOR<sup>y</sup>;  
or when  $Y$  and  $Y'$  are independently selected from -O- and  $-NR^v$ -, then together  
30  $R^{11}$  and  $R^{11}$  are -alkyl-S-S-alkyl- to form a cyclic group, or together  $R^{11}$  and  $R^{11}$  are the  
group:



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, 5 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, 10 alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the 15 phosphorus;
- or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that 20 is three atoms from a Y attached to the phosphorus;
- or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OC(O)CO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,

-SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
 -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

5        Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and  
 aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or  
 together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

10      Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl,  
 alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

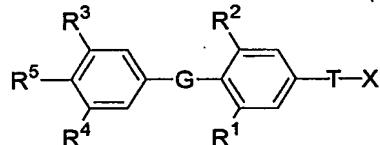
a)      when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each bromo, R<sup>3</sup> is *iso*-propyl, R<sup>4</sup>  
 is hydrogen, and R<sup>5</sup> is -OH, then X is not P(O)(OH)<sub>2</sub> or P(O)(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>;

15      b)      V, Z, W, W' are not all -H; and

c)      when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl,  
 or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically  
 acceptable salts of said prodrugs.

20      97.     The method of claim 83 wherein said phosphonic acid-containing  
 compound is a compound of Formula I:



wherein:

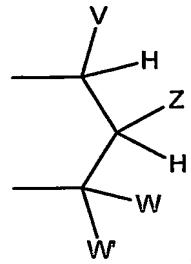
G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-,  
 25 -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;  
 T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
 -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
 30 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-,

- k is an integer from 0-4;  
m is an integer from 0-3;  
n is an integer from 0-2;  
p is an integer from 0-1;
- 5        Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached  
10      to the same C is a hydrogen, or attached via a carbon atom;
- Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;
- Each R<sup>c</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl,  
15      and -C(O)H;
- R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;
- 20      R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>cycloalkyl, optionally substituted (CR<sup>a</sup><sub>2</sub>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>,  
25      , -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>,  
-N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;
- Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;
- 30      Each R<sup>e</sup> is optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;

- R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup>
- 5 and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;
- 10 Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl;
- 15 R<sup>s</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);
- X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;
- Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from
- 20 the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>- OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,
- 25 and -alkyl-S-S-S-alkylhydroxy;
- when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;
- 30 when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>- OC(O)R<sup>y</sup>,

$-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;

- 5 or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



wherein:

- 10 V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- 15 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- 20 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;
- 25 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

5 or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH, 10 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

15 Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxyacryloyloxyalkyl, and lower acyl;

20 with the provisos that:

a) when G is -O-, T is -(CH<sub>2</sub>)<sub>0-4-</sub>, R<sup>1</sup> and R<sup>2</sup> are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH, then X is not -P(O)(OH)<sub>2</sub> or -P(O)(O-lower alkyl)<sub>2</sub>;

25 b) when G is -O-, R<sup>5</sup> is -NHC(O)R<sup>e</sup>, -NHS(=O)<sub>1-2</sub>R<sup>e</sup>, -NHC(S)NH(R<sup>h</sup>), or -NHC(O)NH(R<sup>h</sup>), T is -(CH<sub>2</sub>)<sub>m</sub>-, -CH=CH-, -O(CH<sub>2</sub>)<sub>1-2</sub>-, or -NH(CH<sub>2</sub>)<sub>1-2</sub>-, then X is not -P(O)(OH)<sub>2</sub> or -P(O)(OH)NH<sub>2</sub>;

c) V, Z, W, W' are not all -H; and

30 d) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

98. The method of claim 96 wherein when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each bromo, R<sup>3</sup> is iso-propyl, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.

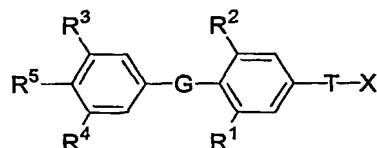
99. The method of claim 97 wherein when G is -O-, T is -(CH<sub>2</sub>)<sub>0-2</sub>, R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen; and wherein when G is -O-, R<sup>5</sup> is selected from the group consisting of NHC(O)R<sup>e</sup>, -NHS(=O)<sub>1-2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>), T is selected from the group consisting of -(CH<sub>2</sub>)<sub>m-</sub>, -CH=CH-, -O(CH<sub>2</sub>)<sub>1-2-</sub>, and -NH(CH<sub>2</sub>)<sub>1-2-</sub>, then R<sup>4</sup> is not hydrogen.

100. A method of activating a thyroid receptor in an animal by administering a phosphonic acid-containing-compound wherein said activation results in the 50% or greater increase in the mRNA expression of a gene selected from the group consisting of LDL receptor, ACC, FAS, spot-14, CPT-1, CYP7A, apo AI, and mGPDH.

101. The method of claim 100 wherein said phosphonic acid-containing-compound binds to a thyroid receptor with a Ki of ≤ 1 μM.

102. The method of claim 101 wherein said phosphonic acid-containing-compound binds to a thyroid receptor with a Ki of ≤ 100 nM.

103. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula I:



wherein:

20 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2-</sub>, -CH<sub>2-</sub>, -CF<sub>2-</sub>, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k-</sub>, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n-</sub>, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n-</sub>, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n-</sub>, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n-</sub>, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n-</sub>, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m-</sub>, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n-</sub>, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p-</sub>;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

30 p is an integer from 0-1;

- Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso
- 5 that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;
- Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;
- 10 Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;
- 15 R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;
- 20 R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>cycloalkyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;
- 25 Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;
- 30 Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;
- R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup>

and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, 5 optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl;

10 R<sup>5</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);

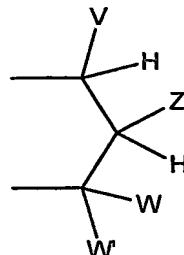
X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;

Y and Y' are each independently selected from the group consisting of -O-, 15 and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, 20 -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, 25 and -cycloalkylene-COOR<sup>y</sup>;

when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, 30 -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from -O- and -NR<sup>V</sup>-, then together R<sup>11</sup> and R<sup>11</sup>' are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup>' are the group:



5 wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

10 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

15 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

20 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

25 or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

5        Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)<sub>2</sub>OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

10      Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

15      Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

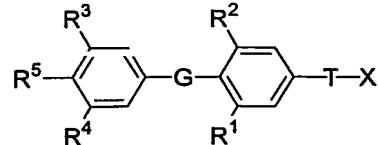
a)     when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each bromo, R<sup>3</sup> is iso-propyl, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH, then X is not P(O)(OH)<sub>2</sub> or P(O)(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>;

20      b)     V, Z, W, W' are not all -H; and

c)     when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

25      104. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula I:



wherein:

30      G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

- T is selected from the group consisting of  $-(CR^a_2)_k-$ ,  $-CR^b=CR^b-(CR^a_2)_n-$ ,  
 $-(CR^a_2)_n-CR^b=CR^b-$ ,  $-(CR^a_2)-CR^b=CR^b-(CR^a_2)-$ ,  $-O(CR^b_2)(CR^a_2)_n-$ ,  
 $-S(CR^b_2)(CR^a_2)_n-$ ,  $-N(R^c)(CR^b_2)(CR^a_2)_n-$ ,  $-N(R^b)C(O)(CR^a_2)_n-$ ,  
 $-(CR^a_2)_nCH(NR^bR^c)-$ ,  $-C(O)(CR^a_2)_m-$ ,  $-(CR^a_2)_mC(O)-$ ,  $-(CR^a_2)C(O)(CR^a_2)_n-$ ,  
5    $-(CR^a_2)_nC(O)(CR^a_2)-$ , and  $-C(O)NH(CR^b_2)(CR^a_2)_p-$ ;
- k is an integer from 0-4;  
m is an integer from 0-3;  
n is an integer from 0-2;  
p is an integer from 0-1;
- 10   Each  $R^a$  is independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_4$  alkyl, halogen, -OH, optionally substituted  $-O-C_1-C_4$  alkyl,  $-OCF_3$ , optionally substituted  $-S-C_1-C_4$  alkyl,  $-NR^bR^c$ , optionally substituted  $-C_2-C_4$  alkenyl, and optionally substituted  $-C_2-C_4$  alkynyl; with the proviso that when one  $R^a$  is attached to C through an O, S, or N atom, then the other  $R^a$  attached  
15   to the same C is a hydrogen, or attached via a carbon atom;
- Each  $R^b$  is independently selected from the group consisting of hydrogen and optionally substituted  $-C_1-C_4$  alkyl;
- Each  $R^c$  is independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_4$  alkyl, optionally substituted  $-C(O)-C_1-C_4$  alkyl,  
20   and  $-C(O)H$ ;
- $R^1$  and  $R^2$  are each independently selected from the group consisting of halogen, optionally substituted  $-C_1-C_4$  alkyl, optionally substituted  $-S-C_1-C_3$  alkyl, optionally substituted  $-C_2-C_4$  alkenyl, optionally substituted  $-C_2-C_4$  alkynyl,  $-CF_3$ ,  $-OCF_3$ , optionally substituted  $-O-C_1-C_3$  alkyl, and cyano;
- 25    $R^3$  and  $R^4$  are each independently selected from the group consisting of hydrogen, halogen,  $-CF_3$ ,  $-OCF_3$ , cyano, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_m$ aryl, optionally substituted  $-(CR^a_2)_m$ cycloalkyl, optionally substituted  $(CR^a_2)_m$ heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-S(=O)_2NR^fR^g$ ,  $-C(O)NR^fR^g$ ,  
30   ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)_2R^e$ ,  $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;
- Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl,

optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;

Each R<sup>e</sup> is optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl,

- 5     optionally substituted -(CR<sup>a</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup>)<sub>n</sub>heterocycloalkyl;

R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally

- 10    substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup> and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>,
- 15    optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl;

- 20    R<sup>s</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);

X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;

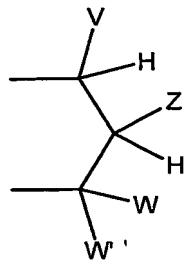
- Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy;
- 25    when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting

of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;

- when Y is -O- and Y' is NR<sup>y</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>y</sup>- is independently selected from the group consisting of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;

- or when Y and Y' are independently selected from -O- and -NR<sup>y</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:

15



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and 20 optionally substituted 1-alkynyl;

- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms 25 from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is

fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one

- 5 substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V

- 10 must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>,  
 15 -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,  
 -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
 -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

- 20 Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

- 25 Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

- a) when G is -O-, T is -(CH<sub>2</sub>)<sub>0-4</sub>-, R<sup>1</sup> and R<sup>2</sup> are independently halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH, then X is not -P(O)(OH)<sub>2</sub> or -P(O)(O-lower alkyl)<sub>2</sub>;  
 30 b) when G is -O-, R<sup>5</sup> is -NHC(O)R<sup>e</sup>, -NHS(=O)<sub>1-2</sub>R<sup>e</sup>, -NHC(S)NH(R<sup>h</sup>), or -NHC(O)NH(R<sup>h</sup>), T is -(CH<sub>2</sub>)<sub>m</sub>-, -CH=CH-, -O(CH<sub>2</sub>)<sub>1-2</sub>-, or -NH(CH<sub>2</sub>)<sub>1-2</sub>-, then X is not -P(O)(OH)<sub>2</sub> or -P(O)(OH)NH<sub>2</sub>;

- c) V, Z, W, W' are not all -H; and
  - d) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;
- and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

5 105. The method of claim 103 wherein when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each bromo, R<sup>3</sup> is *iso*-propyl, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.

106. The method of claim 104 wherein when G is -O-, T is -(CH<sub>2</sub>)<sub>0-2</sub>, R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of halogen, alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or cycloalkyl of 3 to 7 carbons, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen; and wherein when G is -O-, R<sup>5</sup> is selected from the group consisting of NHC(O)R<sup>e</sup>, -NHS(=O)<sub>1-2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>), T is selected from the group consisting of -(CH<sub>2</sub>)<sub>m</sub>-, -CH=CH-, -O(CH<sub>2</sub>)<sub>1-2</sub>-, and -NH(CH<sub>2</sub>)<sub>1-2</sub>-, then R<sup>4</sup> is not hydrogen.

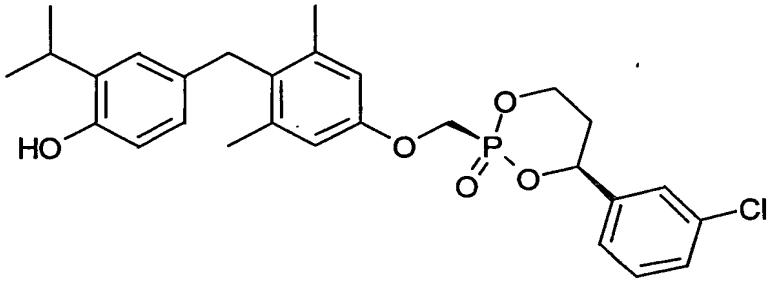
15 107. The method of claim 83 wherein said metabolic disease is NASH.

108. The method of claim 83 wherein said metabolic disease is selected from the group consisting of impaired glucose tolerance, diabetes, and metabolic syndromex.

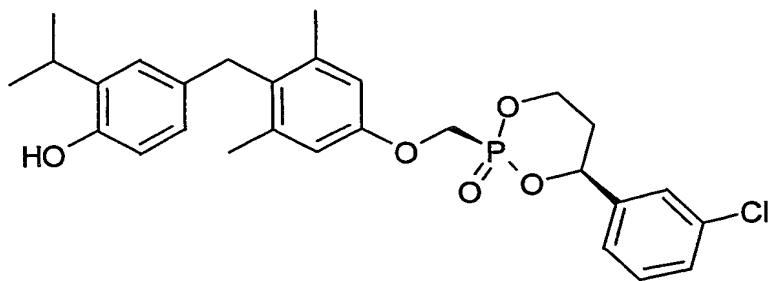
109. The method of claim 96 wherein said metabolic disease is hypercholesterolemia.

20 110. The method of claim 96 wherein said metabolic disease is obesity.

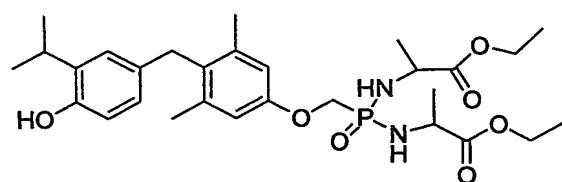
111. The method of claim 109 wherein said compound of Formula I is:



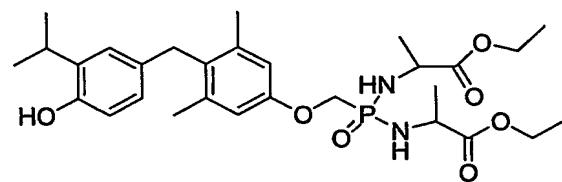
112. The method of claim 110 wherein said compound of Formula I is:



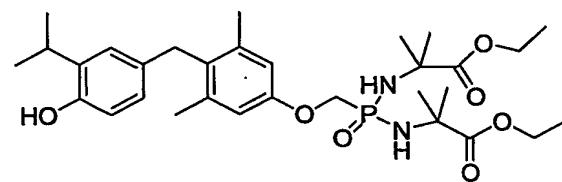
113. The method of claim 109 wherein said compound of Formula I is:



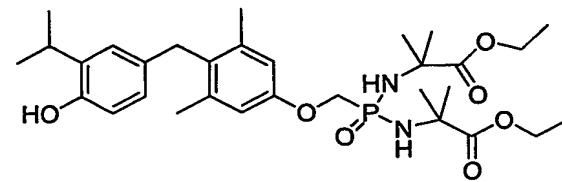
5 114. The method of claim 110 wherein said compound of Formula I is:



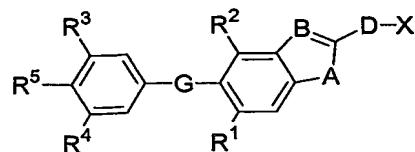
115. The method of claim 109 wherein said compound of Formula I is:



116. The method of claim 110 wherein said compound of Formula I is:



## 117. A compound of Formula II:



wherein:

- A is selected from the group consisting of  $-\text{NR}^i-$ ,  $-\text{O}-$ , and  $-\text{S}-$ ;
- 5      B is selected from the group consisting of  $-\text{CR}^b-$ , and  $-\text{N}-$ ;
- $\text{R}^i$  is selected from the group consisting of hydrogen,  $-\text{C}(\text{O})\text{C}_1\text{-C}_4$  alkyl,  
 $-\text{C}_1\text{-C}_4$  alkyl, and  $-\text{C}_1\text{-C}_4$ -aryl;
- $\text{R}^b$  is selected from the group consisting of hydrogen and optionally  
substituted  $-\text{C}_1\text{-C}_4$  alkyl;
- 10     G is selected from the group consisting of  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{S}(\text{=O})-$ ,  $-\text{S}(\text{=O})_2-$ ,  
 $-\text{CH}_2-$ ,  $-\text{CF}_2-$ ,  $-\text{CHF}-$ ,  $-\text{C}(\text{O})-$ ,  $-\text{CH}(\text{OH})-$ ,  $-\text{NH}-$ , and  $-\text{N}(\text{C}_1\text{-C}_4$  alkyl)-;
- D is selected from the group consisting of a bond,  $-(\text{CR}^a)_2-$ , and  $-\text{C}(\text{O})-$ ;
- Each  $\text{R}^a$  is independently selected from the group consisting of hydrogen,  
optionally substituted  $-\text{C}_1\text{-C}_4$  alkyl, halogen,  $-\text{OH}$ , optionally substituted  $-\text{O-C}_1\text{-C}_4$   
alkyl,  $-\text{OCF}_3$ , optionally substituted  $-\text{S-C}_1\text{-C}_4$  alkyl,  $-\text{NR}^b\text{R}^c$ , optionally  
substituted  $-\text{C}_2\text{-C}_4$  alkenyl, and optionally substituted  $-\text{C}_2\text{-C}_4$  alkynyl; with the proviso  
that when one  $\text{R}^a$  is attached to C through an O, S, or N atom, then the other  $\text{R}^a$  attached  
to the same C is a hydrogen, or attached via a carbon atom;
- 20      $\text{R}^1$  and  $\text{R}^2$  are each independently selected from the group consisting of halogen,  
optionally substituted  $-\text{C}_1\text{-C}_4$  alkyl, optionally substituted  $-\text{S-C}_1\text{-C}_3$  alkyl, optionally  
substituted  $-\text{C}_2\text{-C}_4$  alkenyl, optionally substituted  $-\text{C}_2\text{-C}_4$  alkynyl,  $-\text{CF}_3$ ,  $-\text{OCF}_3$ , optionally  
substituted  $-\text{O-C}_1\text{-C}_3$  alkyl, and cyano;
- $\text{R}^3$  and  $\text{R}^4$  are each independently selected from the group consisting of hydrogen,  
halogen,  $-\text{CF}_3$ ,  $-\text{OCF}_3$ , cyano, optionally substituted  $-\text{C}_1\text{-C}_{12}$  alkyl, optionally  
substituted  $-\text{C}_2\text{-C}_{12}$  alkenyl, optionally substituted  $-\text{C}_2\text{-C}_{12}$  alkynyl, optionally  
substituted  $-(\text{CR}^a)_m\text{aryl}$ , optionally substituted  $-(\text{CR}^a)_m\text{cycloalkyl}$ , optionally  
substituted  $-(\text{CR}^a)_m\text{heterocycloalkyl}$ ,  $-\text{OR}^d$ ,  $-\text{SR}^d$ ,  $-\text{S}(\text{=O})\text{R}^e$ ,  $-\text{S}(\text{=O})_2\text{R}^e$ ,  $-\text{S}(\text{=O})_2\text{NR}^f\text{R}^g$ ,  
 $-\text{C}(\text{O})\text{NR}^f\text{R}^g$ ,  $-\text{C}(\text{O})\text{OR}^h$ ,  $-\text{C}(\text{O})\text{R}^e$ ,  $-\text{N}(\text{R}^b)\text{C}(\text{O})\text{R}^e$ ,  $-\text{N}(\text{R}^b)\text{C}(\text{O})\text{NR}^f\text{R}^g$ ,  $-\text{N}(\text{R}^b)\text{S}(\text{=O})_2\text{R}^e$ ,  
 $-\text{N}(\text{R}^b)\text{S}(\text{=O})_2\text{NR}^f\text{R}^g$ , and  $-\text{NR}^f\text{R}^g$ ;

Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;

5        Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup>)<sub>n</sub>heterocycloalkyl;

10      R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup> and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said 15      optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

16      Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, 20      optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl;

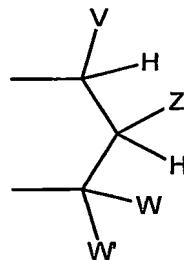
17      R<sup>s</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);

25      X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;

26      Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-, when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety 30      contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy;

when Y and Y' are  $-NR^V-$ , then  $R^{11}$  attached to  $-NR^V-$  is independently selected from the group consisting of  $-H$ ,  $-[C(R^Z)_2]_q-COOR^Y$ ,  $-C(R^X)_2COOR^Y$ ,  $-[C(R^Z)_2]_q-C(O)SR^Y$ , and  $-cycloalkylene-COOR^Y$ ;

- 5        when Y is  $-O-$  and Y' is  $NR^V$ , then  $R^{11}$  attached to  $-O-$  is independently selected from the group consisting of  $-H$ , alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted  $CH_2$ -heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^Z)_2OC(O)NR^Z_2$ ,  $-NR^Z-C(O)-R^Y$ ,  $-C(R^Z)_2-OC(O)R^Y$ ,  $-C(R^Z)_2-O-C(O)OR^Y$ ,  $-C(R^Z)_2OC(O)SR^Y$ , -alkyl-S-C(O)R<sup>Y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy; and  $R^{11}$  attached to  $-NR^V-$  is independently selected from the group consisting of  $-H$ ,  $-[C(R^Z)_2]_q-COOR^Y$ ,  $-C(R^X)_2COOR^Y$ ,  $-[C(R^Z)_2]_q-C(O)SR^Y$ , and  $-cycloalkylene-COOR^Y$ ;
- 10      or when Y and Y' are independently selected from  $-O-$  and  $-NR^V-$ , then together  $R^{11}$  and  $R^{11}$  are -alkyl-S-S-alkyl- to form a cyclic group, or together  $R^{11}$  and  $R^{11}$  are the group:



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- 20      or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- 25      or together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

5 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

10 or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

15 or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

25 Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

30 a) V, Z, W, W' are not all -H; and

b) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

118. The compound of claim 117 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-.

119. The compound of claim 117 wherein D is selected from the group consisting of a bond and -CH<sub>2</sub>-.

5 120. The compound of claim 117 wherein A is selected from the group consisting of -NH-, -NMe-, -O-, and -S-.

121. The compound of claim 117 wherein B is selected from the group consisting of -CH<sub>2</sub>-, CMe-, and -N-.

10 122. The compound of claim 117 wherein R<sup>1</sup> and R<sup>2</sup> are the same and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.

123. The compound of claim 117 wherein R<sup>1</sup> and R<sup>2</sup> are different and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.

124. The compound of claim 117 wherein R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano and CF<sub>3</sub>.

15 125. The compound of claim 117 wherein R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>.

126. The compound of claim 117 wherein R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>.

20 127. The compound of claim 117 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>], and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

25 128. The compound of claim 117 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-; D is selected from the group consisting of a bond and -CH<sub>2</sub>-; A is selected from the group consisting of -NH-, -NMe-, -O-, and -S-; B is selected from the group consisting of -CH-, -CMe-, and -N-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano and CF<sub>3</sub>; R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>; and X is selected from the group

consisting of  $-\text{PO}_3\text{H}_2$ ,  $-\text{P}(\text{O})[-\text{OCR}^z_2\text{OC(O)R}^y]_2$ ,  
 $-\text{P}(\text{O})[-\text{OCR}^z_2\text{OC(O)OR}^y]_2$ ,  $-\text{P}(\text{O})[-\text{N(H)}\text{CR}^z_2\text{C(O)OR}^y]_2$ ,  
 $-\text{P}(\text{O})[-\text{N(H)}\text{CR}^z_2\text{C(O)OR}^y][-\text{OR}^{11}]$  and  $-\text{P}(\text{O})[-\text{OCH(V)}\text{CH}_2\text{CH}_2\text{O}-]$ , wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and  
5       optionally substituted heteroaryl.

129. The compound of claim 128 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>; D is selected from the group consisting of a bond and -CH<sub>2</sub>-; A is selected from the group consisting of -NH-, -NMe-, -O-, and -S-; B is selected from the group consisting of -CH-, -CMe- and -N-; R<sup>1</sup> and R<sup>2</sup> are each independently selected  
10      from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and halogen; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; and R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is  
15      selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl.

130. The compound of claim 129 wherein G is -O-; D is a bond; A is selected  
20      from the group consisting of -NH- and -NMe-; B is selected from the group consisting of -CH- and -CMe-; R<sup>1</sup> and R<sup>2</sup> are each bromo; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is -OH; and R<sup>3</sup> is isopropyl.

131. The compound of claim 130 wherein X is selected from the group consisting of  $-\text{PO}_3\text{H}_2$ ,  $-\text{P}(\text{O})[-\text{OCH}_2\text{OC(O)-}t\text{-butyl}]_2$ ,  $-\text{P}(\text{O})[-\text{OCH}_2\text{OC(O)O-}i\text{-propyl}]_2$ ,  
25       $-\text{P}(\text{O})[-\text{N(H)}\text{CH(CH}_3\text{)C(O)OCH}_2\text{CH}_3]_2$ ,  $-\text{P}(\text{O})[-\text{N(H)}\text{C(CH}_3)_2\text{C(O)OCH}_2\text{CH}_3]_2$ ,  
 $-\text{P}(\text{O})[-\text{N(H)}\text{CH(CH}_3\text{)C(O)OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$ ,  
 $-\text{P}(\text{O})[-\text{N(H)}\text{C(CH}_3)_2\text{C(O)OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$ ,  
and  $-\text{P}(\text{O})[-\text{OCH(3-chlorophenyl)}\text{CH}_2\text{CH}_2\text{O}-]$ .

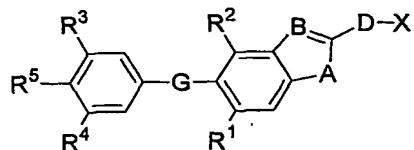
132. The compound of claim 129 wherein G is -O-; D is a bond; A is -O-; B is selected from the group consisting of -CH- and -CMe-; R<sup>1</sup> and R<sup>2</sup> are each bromo; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is -OH; and R<sup>3</sup> is isopropyl.  
30

133. The compound of claim 132 wherein X is selected from the group consisting of  $-\text{PO}_3\text{H}_2$ ,  $-\text{P}(\text{O})[-\text{OCH}_2\text{OC(O)-}t\text{-butyl}]_2$ ,  $-\text{P}(\text{O})[-\text{OCH}_2\text{OC(O)O-}i\text{-propyl}]_2$ ,  
 $-\text{P}(\text{O})[-\text{N(H)}\text{CH(CH}_3\text{)C(O)OCH}_2\text{CH}_3]_2$ ,  $-\text{P}(\text{O})[-\text{N(H)}\text{C(CH}_3)_2\text{C(O)OCH}_2\text{CH}_3]_2$ ,

-P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
 -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
 and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

134. The compound as in any of claims 117, 128, 129, 131, and 133 wherein X  
 5 is -PO<sub>3</sub>H<sub>2</sub>.

135. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula II:



wherein:

- 10        A is selected from the group consisting of -NR<sup>i</sup>-, -O-, and -S-;
- B is selected from the group consisting of -CR<sup>b</sup>-, and -N-;
- R<sup>i</sup> is selected from the group consisting of hydrogen, -C(O)C<sub>1</sub>-C<sub>4</sub> alkyl, -C<sub>1</sub>-C<sub>4</sub> alkyl, and -C<sub>1</sub>-C<sub>4</sub>-aryl;
- R<sup>b</sup> is selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;
- 15        G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;
- D is selected from the group consisting of a bond, -(CR<sup>a</sup>)<sub>2</sub>-, and -C(O)-;
- Each R<sup>a</sup> is independently selected from the group consisting of hydrogen,
- 20        optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;
- 25        R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;
- R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen,
- 30        halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally

substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>cycloalkyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, 5 -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;

Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;

10 Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;

15 R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup> and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said 20 optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

25 Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;

30 X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;

R<sup>s</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);

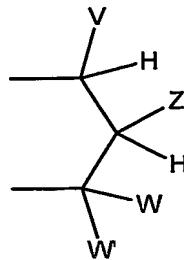
Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety

contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy;

5 when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

10 when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

15 or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining

atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

5        or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

10      or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

15      or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

20      Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

25      q is an integer 2 or 3;

Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

30      Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

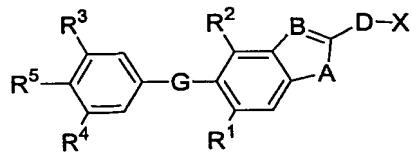
with the provisos that:

a)      V, Z, W, W' are not all -H; and

b) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

5 136. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula II:



wherein:

A is selected from the group consisting of -NR<sup>i</sup>-, -O-, and -S-;

10 B is selected from the group consisting of -CR<sup>b</sup>-, and -N-;

R<sup>i</sup> is selected from the group consisting of hydrogen, -C(O)C<sub>1</sub>-C<sub>4</sub> alkyl, -C<sub>1</sub>-C<sub>4</sub> alkyl, and -C<sub>1</sub>-C<sub>4</sub>-aryl;

R<sup>b</sup> is selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

15 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

D is selected from the group consisting of a bond, -(CR<sup>a</sup>)<sub>2</sub>-, and -C(O)-;

Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;

25 R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;

30 R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally

substituted  $-(CR^a_2)_m$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, optionally substituted  $-(CR^a_2)_m$ heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-S(=O)_2NR^fR^g$ ,  $-C(O)NR^fR^g$ ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)R^e$ ,  $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;

5        Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, and  $-C(O)NR^fR^g$ ;

10      Each  $R^e$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_n$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, and optionally substituted  $-(CR^a_2)_n$ heterocycloalkyl;

15       $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected 20 from the group consisting of optionally substituted  $-C_1-C_4$  alkyl,  $-OR^b$ , oxo, cyano,  $-CF_3$ , optionally substituted phenyl, and  $-C(O)OR^h$ ;

25      Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

30       $R^5$  is selected from the group consisting of  $-OH$ , optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ ,  $-F$ ,  $-NHC(O)R^e$ ,  $-NHS(=O)R^e$ ,  $-NHS(=O)_2R^e$ ,  $-NHC(=S)NH(R^h)$ , and  $-NHC(O)NH(R^h)$ ;

35      X is  $P(O)YR^{11}Y'R^{11}$ ;

40      Y and Y' are each independently selected from the group consisting of  $-O-$ , and  $-NR^v-$ ; when Y and Y' are  $-O-$ , R<sup>11</sup> attached to  $-O-$  is independently selected from the group consisting of  $-H$ , alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,

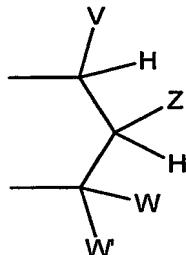
-C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>,  
 -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
 and -alkyl-S-S-alkylhydroxy;

when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected

- 5 from the group consisting  
 of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>,  
 and -cycloalkylene-COOR<sup>y</sup>;

- when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected  
 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted  
 10 heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety  
 contains a carbonate or thiocarbonate, optionally  
 substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>,  
 -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
 and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from  
 15 the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>,  
 and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together  
 R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the  
 group:



20

wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen,  
 optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,  
 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and  
 25 optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic  
 group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining  
 atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

10      or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

15      or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)<sub>2</sub>OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

25      Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

30      Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

a)      V, Z, W, W' are not all -H; and

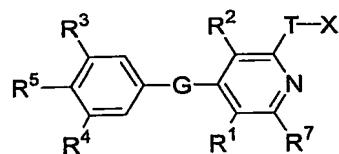
b)      when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

137. The method of claim 135 wherein said metabolic disease is hypercholesterolemia.

5 138. The method of claim 135 wherein said metabolic disease is obesity.

139. A compound of Formula III:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-,

10 -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,

-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-,

-O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,

-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,

15 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-;

k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

20 Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;

25 Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl,

30 and -C(O)H;

$R^1$  and  $R^2$  are each independently selected from the group consisting of halogen, optionally substituted  $-C_1-C_4$  alkyl, optionally substituted  $-S-C_1-C_3$  alkyl, optionally substituted  $-C_2-C_4$  alkenyl, optionally substituted  $-C_2-C_4$  alkynyl,  $-CF_3$ ,  $-OCF_3$ , optionally substituted  $-O-C_1-C_3$  alkyl, and cyano;

- 5        $R^3$  and  $R^4$  are each independently selected from the group consisting of hydrogen, halogen,  $-CF_3$ ,  $-OCF_3$ , cyano, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_m$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, optionally substituted  $-(CR^a_2)_m$ heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-S(=O)_2NR^fR^g$ ,  
10       $-C(O)NR^fR^g$ ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)_2R^e$ ,  
 $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;

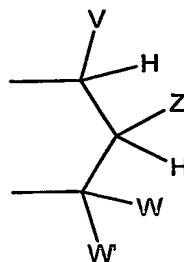
15      Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, and  $-C(O)NR^fR^g$ ;

20      Each  $R^e$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_n$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, and optionally substituted  $-(CR^a_2)_n$ heterocycloalkyl;

25       $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O,  $NR^c$ , and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted  $-C_1-C_4$  alkyl,  $-OR^b$ , oxo, cyano,  $-CF_3$ , optionally substituted phenyl, and  $-C(O)OR^h$ ;

30      Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

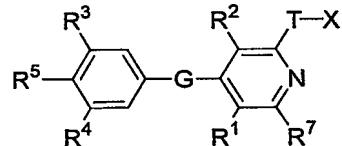
- R<sup>5</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);
- R<sup>7</sup> is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl;
- 5 X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;
- Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;
- 10 when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;
- 15 when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;
- 20 or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:
- 25
- 30



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, 5 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,
- 10 alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the
- 15 phosphorus;
- or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;
- 20 or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,

- SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
 -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;
- q is an integer 2 or 3;
- 5        Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;  
 Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;  
 Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;
- 10      Each R<sup>y</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;  
 with the provisos that:  
 a)        when G is -O-, T is -NH-CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each chloro, R<sup>3</sup> is iso-propyl, R<sup>4</sup> is hydrogen, R<sup>7</sup> is fluoro, and R<sup>5</sup> is -OH, then X is not P(O)(OH)<sub>2</sub>,  
 15      P(O)(OH)(OCH<sub>3</sub>) or P(O)(OCH<sub>3</sub>)<sub>2</sub>;  
 b)        V, Z, W, W' are not all -H; and  
 c)        when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;  
 and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.
- 20      140. A compound of Formula III:



wherein:

- G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-,  
 25      -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;  
 T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-,  
 -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
 30      -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-;

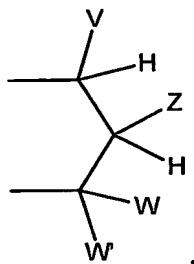
- k is an integer from 0-4;  
m is an integer from 0-3;  
n is an integer from 0-2;  
p is an integer from 0-1;
- 5        Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached  
10 to the same C is a hydrogen, or attached via a carbon atom;
- Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;
- Each R<sup>c</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl,  
15 and -C(O)H;
- R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;
- 20        R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>cycloalkyl, optionally substituted (CR<sup>a</sup>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>,  
25 , -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;
- Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;
- Each R<sup>e</sup> is optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup>)<sub>n</sub>heterocycloalkyl;

- $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b)_n$ aryl, optionally substituted  $-(CR^b)_n$ cycloalkyl, and optionally substituted  $-(CR^b)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted  $-C_1-C_4$  alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;
- 10        Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b)_n$ aryl, optionally substituted  $-(CR^b)_n$ cycloalkyl, and optionally substituted  $-(CR^b)_n$ heterocycloalkyl;
- 15         $R^5$  is selected from the group consisting of -OH, optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ , -F,  $-NHC(O)R^e$ ,  $-NHS(=O)R^e$ ,  $-NHS(=O)_2R^e$ ,  $-NHC(=S)NH(R^h)$ , and  $-NHC(O)NH(R^h)$ ;
- 20         $R^7$  is selected from the group consisting of hydrogen, halogen, amino, hydroxyl,  $-O-C_1-C_4$  alkyl, -SH and  $-S-C_1-C_4$  alkyl;
- 25        X is  $P(O)YR^{11}Y'R^{11}$ ;
- 20        Y and Y' are each independently selected from the group consisting of -O-, and  $-NR^v-$ ; when Y and Y' are  $-O-$ ,  $R^{11}$  attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;
- 30        when Y and Y' are  $-NR^v-$ , then  $R^{11}$  attached to  $-NR^v-$  is independently selected from the group consisting of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;
- 35        when Y is -O- and Y' is NR<sup>y</sup>, then  $R^{11}$  attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety

contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^{z_2}$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from

5 the group consisting of -H,  $[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



10

wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and

15 optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms

20 from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

25 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy,

alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W' are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V

5 must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>,  
10 -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,  
-SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
-R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
-(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

15 Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

20 Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -C(O)- and -NR<sup>b</sup>-; T is -A-B- where A is selected from the group  
25 consisting of  
-NR<sup>b</sup>-, -O-, -CH<sub>2</sub>- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl; R<sup>3</sup> is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl,

and substituted or unsubstituted C<sub>3</sub>-C<sub>5</sub> cycloalkyl; R<sup>7</sup> is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl; and R<sup>5</sup> is selected from the group consisting of hydroxyl, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, and -OC(O)R<sup>e</sup>; then X is not -P(O)(OH)<sub>2</sub>;

- 5        b)      V, Z, W, W' are not all -H; and  
          c)      when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

10      141. The compound of claim 139 wherein when G is -O-, T is -NH-CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each chloro, R<sup>3</sup> is *iso*-propyl, R<sup>7</sup> is fluoro and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.

15      142. The compound of claim 140 wherein when G is selected from the group consisting of oxygen, sulfur, sulfoxide, sulfonyl, -CH<sub>2</sub>-, -C(O)- and -NR<sup>b</sup>-; T is -A-B- where A is selected from the group consisting of -NR<sup>b</sup>-, -O-, -CH<sub>2</sub>- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl; R<sup>3</sup> is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, and substituted or unsubstituted C<sub>3</sub>-C<sub>5</sub> cycloalkyl; and R<sup>7</sup> is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl; then R<sup>5</sup> is not hydroxyl, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, or -OC(O)R<sup>e</sup>.

20      143. The compound of claim 139 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-.

25      144. The compound of claim 140 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-.

145. The compound of claim 139 wherein T is selected from the group consisting of  $-(CR^a_2)_n-$ ,  $-O(CR^b_2)(CR^a_2)_p-$ ,  $-N(R^c)(CR^b_2)(CR^a_2)_p-$ ,  $-S(CR^b_2)(CR^a_2)_p-$ ,  $-NR^b(CO)-$ , and  $-CH_2CH(NR^cR^b)-$ .

146. The compound of claim 140 wherein T is selected from the group consisting of  $-(CR^a_2)_n-$ ,  $-O(CR^b_2)(CR^a_2)_p-$ ,  $-N(R^c)(CR^b_2)(CR^a_2)_p-$ ,  $-S(CR^b_2)(CR^a_2)_p-$ ,  $-NR^b(CO)-$ , and  $-CH_2CH(NR^cR^b)-$ .

147. The compound of claim 139 wherein R<sup>1</sup> and R<sup>2</sup> are the same and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.

148. The compound of claim 140 wherein R<sup>1</sup> and R<sup>2</sup> are the same and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.

149. The compound of claim 139 wherein R<sup>1</sup> and R<sup>2</sup> are different and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.

150. The compound of claim 140 wherein R<sup>1</sup> and R<sup>2</sup> are different and are selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano.

151. The compound of claim 139 wherein R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano and CF<sub>3</sub>.

152. The compound of claim 140 wherein R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano, and CF<sub>3</sub>.

153. The compound of claim 139 wherein R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>.

154. The compound of claim 140 wherein R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>.

155. The compound of claim 139 wherein R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>.

156. The compound of claim 140 wherein R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>.

157. The compound of claim 139 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>], and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

158. The compound of claim 140 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>], and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of 5 optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

159. The compound of claim 139 wherein R<sup>7</sup> is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and -O-CH<sub>3</sub>.

160. The compound of claim 140 wherein R<sup>7</sup> is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and -O-CH<sub>3</sub>.

161. The compound of claim 139 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-; T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -NR<sup>b</sup>(CO)-, and -CH<sub>2</sub>CH(NR<sup>c</sup>R<sup>b</sup>); R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano; R<sup>4</sup> is selected from the group 15 consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano and CF<sub>3</sub>; R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>; R<sup>7</sup> is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and -O-CH<sub>3</sub>; and X is selected from the group consisting 20 of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>] and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of optionally substituted aryl, aryl, heteroaryl, and 25 optionally substituted heteroaryl.

162. The compound of claim 161 wherein when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are chloro, R<sup>3</sup> is *iso*-propyl, R<sup>7</sup> is fluoro, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.

163. The compound of claim 140 wherein G is selected from the group consisting of -O- and -CH<sub>2</sub>-; T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-, -NR<sup>b</sup>(CO)-, and -CH<sub>2</sub>CH(NR<sup>c</sup>R<sup>b</sup>); R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group 30 consisting of halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, -CF<sub>3</sub>, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, -C<sub>1</sub>-C<sub>4</sub> alkyl, cyano, and CF<sub>3</sub>; R<sup>5</sup> is selected from the group consisting of -OH, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, and -NHC(O)R<sup>e</sup>; R<sup>3</sup> is selected

from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, -CF<sub>3</sub>, cyano, -C(O)NR<sup>f</sup>R<sup>g</sup>, optionally substituted (CR<sup>a</sup>)<sub>n</sub>aryl, -SO<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -SO<sub>2</sub>R<sup>e</sup>; R<sup>7</sup> is selected from the group consisting of hydrogen, fluoro, chloro, amino, hydroxyl, and -O-CH<sub>3</sub>; and X is selected from the group consisting

- 5 of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCR<sup>z</sup>OC(O)R<sup>y</sup>]<sub>2</sub>, -P(O)[-OCR<sup>z</sup><sub>2</sub>OC(O)OR<sup>y</sup>]<sub>2</sub>,  
 -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>]<sub>2</sub>, -P(O)[-N(H)CR<sup>z</sup><sub>2</sub>C(O)OR<sup>y</sup>][-OR<sup>11</sup>],  
 and -P(O)[-OCH(V)CH<sub>2</sub>CH<sub>2</sub>O-], wherein V is selected from the group consisting of  
 optionally substituted aryl, aryl, heteroaryl, and optionally substituted heteroaryl.

164. The compound of claim 163 wherein when G is selected from the group  
 10 consisting of -O- and -CH<sub>2</sub>-; T is -A-B- where A is selected from the group consisting  
 of -NR<sup>b</sup>-, -O-, -CH<sub>2</sub>- and -S- and B is selected from the group consisting of a bond and  
 substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl; R<sup>3</sup> is selected from the group consisting of  
 halogen, trifluoromethyl, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or  
 unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide,  
 15 sulfone, sulfonamide and C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl  
 ring(s) are attached or fused to the aromatic; R<sup>4</sup> is selected from the group consisting of  
 hydrogen, halogen, and substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl; R<sup>1</sup> and R<sup>2</sup> are each  
 independently selected from the group consisting of halogen and substituted or  
 unsubstituted -C<sub>1</sub>-C<sub>4</sub> alkyl; and R<sup>7</sup> is selected from the group consisting of hydrogen,  
 20 fluoro, chloro, amino, hydroxyl, and -O-CH<sub>3</sub>; then R<sup>5</sup> is not hydroxyl, optionally  
 substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, or -OC(O)R<sup>e</sup>.

165. The compound of claim 161 wherein T is -N(H)C(O)-; R<sup>1</sup> and R<sup>2</sup> are each  
 independently selected from the group consisting of iodo, bromo, chloro, methyl, and  
 cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from  
 25 the group consisting of -OH and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of  
 iodo, bromo, optionally substituted -C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl,  
 optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido  
 group is selected from the group consisting of phenethylamino, piperidinyl,  
 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup>  
 30 wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl,  
 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen  
 and fluoro.

166. The compound of claim 165 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro;  
 R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; R<sup>7</sup> is fluoro; and R<sup>3</sup> is -iso-propyl.

167. The compound of claim 166 wherein X is selected from the group consisting of  $\text{-PO}_3\text{H}_2$ ,  $\text{-P(O)[-OCH}_2\text{OC(O)-}t\text{-butyl]}_2$ ,  $\text{-P(O)[-OCH}_2\text{OC(O)O-}i\text{-propyl]}_2$ ,  $\text{-P(O)[-N(H)CH(CH}_3\text{)C(O)OCH}_2\text{CH}_3]_2$ ,  $\text{-P(O)[-N(H)C(CH}_3\text{)}_2\text{C(O)OCH}_2\text{CH}_3]_2$ ,  $\text{-P(O)[-N(H)CH(CH}_3\text{)C(O)OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$ ,  
5  $\text{-P(O)[-N(H)C(CH}_3\text{)}_2\text{C(O)OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$ ,  
and  $\text{-P(O)[-OCH(3-chlorophenyl)CH}_2\text{CH}_2\text{O-]}$ .

168. The compound of claim 161 wherein T is  $\text{-OCH}_2\text{-}$ ; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from 10 the group consisting of  $\text{-OH}$ , and  $\text{-OC(O)R}^e$ ; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted  $\text{-CH}_2\text{aryl}$ , optionally substituted  $\text{-CH(OH)aryl}$ ,  $\text{-C(O)-amido}$ ,  $\text{-S(=O)}_2\text{-amido}$ , wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and  $\text{-SO}_2\text{R}^e$  15 wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

169. The compound of claim 168 wherein G is  $\text{-O-}$ ; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>7</sup> is fluoro; R<sup>5</sup> is  $\text{-OH}$ ; and R<sup>3</sup> is *iso*-propyl.

170. The compound of claim 169 wherein X is selected from the group consisting of  $\text{-PO}_3\text{H}_2$ ,  $\text{-P(O)[-OCH}_2\text{OC(O)-}t\text{-butyl]}_2$ ,  $\text{-P(O)[-OCH}_2\text{OC(O)O-}i\text{-propyl]}_2$ ,  $\text{-P(O)[-N(H)CH(CH}_3\text{)C(O)OCH}_2\text{CH}_3]_2$ ,  $\text{-P(O)[-N(H)C(CH}_3\text{)}_2\text{C(O)OCH}_2\text{CH}_3]_2$ ,  $\text{-P(O)[-N(H)CH(CH}_3\text{)C(O)OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$ ,  $\text{-P(O)[-N(H)C(CH}_3\text{)}_2\text{C(O)OCH}_2\text{CH}_3][3,4\text{-methylenedioxyphenyl}]$ ,  
25 and  $\text{-P(O)[-OCH(3-chlorophenyl)CH}_2\text{CH}_2\text{O-]}$ .

171. The compound of claim 161 wherein T is  $\text{-CH}_2\text{-}$ ; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from 30 the group consisting of  $\text{-OH}$ , and  $\text{-OC(O)R}^e$ ; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted  $\text{-CH}_2\text{aryl}$ , optionally substituted  $\text{-CH(OH)aryl}$ ,  $\text{-C(O)-amido}$ ,  $\text{-S(=O)}_2\text{-amido}$  wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and  $\text{-SO}_2\text{R}^e$  wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl,

4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

172. The compound of claim 171 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *i*-propyl.

5 173. The compound of claim 172 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], 10 and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

174. The compound of claim 161 wherein T is -CH<sub>2</sub>CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of 15 iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 20 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

175. The compound of claim 174 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

176. The compound of claim 175 wherein X is selected from the group 25 consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

30 177. The compound of claim 161 wherein T is -NHCH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH, and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl,

optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

5        178. The compound of claim 177 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl, then R<sup>4</sup> is not hydrogen.

10      179. The compound of claim 177 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each bromo; R<sup>4</sup> is hydrogen; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

180. The compound of claim 179 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxophenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxophenyl], and -P(O)[-OCH(3-chlorophenyl) CH<sub>2</sub>CH<sub>2</sub>O-].

181. The compound of claim 163 wherein T is -N(H)C(O)-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

182. The compound of claim 181 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>7</sup> is fluoro; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

183. The compound of claim 181 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxophenyl],

-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

184. The compound of claim 163 wherein T is -OCH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl,  
 5 10 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

185. The compound of claim 184 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

186. The compound of claim 184 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

187. The compound of claim 163 wherein T is -CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl,  
 25 30 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

188. The compound of claim 187 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>7</sup> is fluoro; R<sup>4</sup> is hydrogen; R<sup>5</sup> is -OH; and R<sup>3</sup> is *i*-propyl.

189. The compound of claim 187 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]₂, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]₂,  
5 -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]₂, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]₂,  
-P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O) OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

190. The compound of claim 163 wherein T is -CH<sub>2</sub>CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl, optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl, 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

191. The compound of claim 190 wherein G is -O-; T is -CH<sub>2</sub>CH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>4</sup> is hydrogen; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

192. The compound of claim 190 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]₂, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]₂,  
-P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]₂, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]₂,  
-P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
-P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O) OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl],  
and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

193. The compound of claim 163 wherein T is -NHCH<sub>2</sub>-; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of iodo, bromo, chloro, methyl, and cyano; R<sup>4</sup> is selected from the group consisting of hydrogen and iodo; R<sup>5</sup> is selected from the group consisting of -OH and -OC(O)R<sup>e</sup>; R<sup>3</sup> is selected from the group consisting of iodo, bromo, optionally substituted C<sub>1</sub>-C<sub>6</sub> alkyl, optionally substituted -CH<sub>2</sub>aryl,

optionally substituted -CH(OH)aryl, -C(O)-amido, -S(=O)<sub>2</sub>-amido, wherein the amido group is selected from the group consisting of phenethylamino, piperidinyl, 4-methylpiperizinyl, morpholinyl, cyclohexylamino, anilinyl, and indolinyl, and -SO<sub>2</sub>R<sup>e</sup> wherein R<sup>e</sup> is selected from the group consisting of phenyl, 4-chlorophenyl,

- 5 4-fluorophenyl, and 4-pyridyl; and R<sup>7</sup> is selected from the group consisting of hydrogen and fluoro.

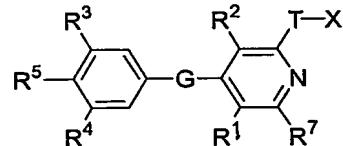
194. The compound of claim 193 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each chloro; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl, then R<sup>4</sup> is not hydrogen

- 10 195. The compound of claim 193 wherein G is -O-; R<sup>1</sup> and R<sup>2</sup> are each bromo; R<sup>4</sup> is hydrogen; R<sup>7</sup> is fluoro; R<sup>5</sup> is -OH; and R<sup>3</sup> is *iso*-propyl.

196. The compound of claim 195 wherein X is selected from the group consisting of -PO<sub>3</sub>H<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)-*t*-butyl]<sub>2</sub>, -P(O)[-OCH<sub>2</sub>OC(O)O-*i*-propyl]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>, -P(O)[-N(H)CH(CH<sub>3</sub>)C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], -P(O)[-N(H)C(CH<sub>3</sub>)<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>][3,4-methylenedioxyphenyl], and -P(O)[-OCH(3-chlorophenyl)CH<sub>2</sub>CH<sub>2</sub>O-].

15 197. The compound as in any of claims 139, 140, 141, 142, 161, 163, 165, 167, 168, 170, 171, 173, 174, 176, 177, 180, 181, 183, 184, 186, 187, 189, 190, or 193, wherein X is -PO<sub>3</sub>H<sub>2</sub>.

20 198. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

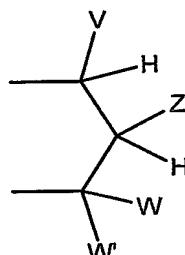
- G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;
- 25 T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, 30 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-;

- k is an integer from 0-4;  
m is an integer from 0-3;  
n is an integer from 0-2;  
p is an integer from 0-1;
- 5        Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached  
10      to the same C is a hydrogen, or attached via a carbon atom;
- Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;
- Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;
- 15      R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;
- 20      R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>cycloalkyl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>,  
25      -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;
- Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;
- 30      Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup>)<sub>n</sub>heterocycloalkyl;

- $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$
- 5     and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted  $-C_1-C_4$  alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;
- 10    Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;
- 15     $R^5$  is selected from the group consisting of -OH, optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ , -F,  $-NHC(O)R^e$ ,  $-NHS(=O)R^e$ ,  $-NHS(=O)_2R^e$ ,  $-NHC(=S)NH(R^h)$ , and  $-NHC(O)NH(R^h)$ ;
- 20     $R^7$  is selected from the group consisting of hydrogen, halogen, amino, hydroxyl,  $-O-C_1-C_4$  alkyl, -SH and  $-S-C_1-C_4$  alkyl;
- 25    X is  $P(O)YR^{11}Y'R^{11}$ ;
- 30    Y and Y' are each independently selected from the group consisting of -O-, and  $-NR^v-$ ; when Y and Y' are  $-O-$ ,  $R^{11}$  attached to  $-O-$  is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;
- 35    when Y and Y' are  $-NR^v-$ , then  $R^{11}$  attached to  $-NR^v-$  is independently selected from the group consisting of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;
- 40    when Y is  $-O-$  and Y' is  $NR^v$ , then  $R^{11}$  attached to  $-O-$  is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety

contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  
 $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  
 $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>y</sup>- is independently selected from  
5 the group consisting of -H,  $[C(R^z)_2]_q-COOR^y$ ,  $C(R^x)_2COOR^y$ ,  $[C(R^z)_2]_q-C(O)SR^y$ ,  
and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from -O- and -NR<sup>y</sup>-, then together  
R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the  
group:



10

wherein:

V, W, and W' are independently selected from the group consisting of hydrogen,  
optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,  
substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and  
15 optionally substituted 1-alkynyl;

or together V and Z are connected via an additional 3-5 atoms to form a cyclic  
group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining  
atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,  
alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms  
20 from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic  
group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is  
fused to an aryl group at the beta and gamma position to the Y attached to the  
phosphorus;

25 or together V and W are connected via an additional 3 carbon atoms to form an  
optionally substituted cyclic group containing 6 carbon atoms and substituted with one  
substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy,

alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V

5 must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>,  
 10 -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,  
 -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)<sub>2</sub>OH, -CH(C≡CR<sup>z</sup>)OH,  
 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
 -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

15 Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

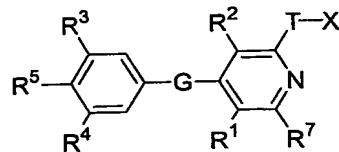
Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

20 Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

- a) when G is -O-, T is -NH-CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each chloro, R<sup>3</sup> is iso-propyl, R<sup>4</sup> is hydrogen, R<sup>7</sup> is fluoro, and R<sup>5</sup> is -OH, then X is not P(O)(OH)<sub>2</sub>,
  - 25 P(O)(OH)(OCH<sub>3</sub>) or P(O)(OCH<sub>3</sub>)<sub>2</sub>;
  - b) V, Z, W, W' are not all -H; and
  - c) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;
- and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

30 199. The method of claim 83 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

5        T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>;

10      k is an integer from 0-4;

        m is an integer from 0-3;

        n is an integer from 0-2;

        p is an integer from 0-1;

        Each R<sup>a</sup> is independently selected from the group consisting of hydrogen,

15      optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;

20      Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

        Each R<sup>c</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;

25      R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;

30      R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally

substituted  $-(CR^a_2)_m$ aryl, optionally substituted  $-(CR^a_2)_m$ cycloalkyl, optionally substituted  $(CR^a_2)_m$ heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-C(O)NR^fR^g$ ,  $-C(O)NR^fR^g$ ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)_2R^e$ ,  $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;

5        Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, and  $-C(O)NR^fR^g$ ;

10      Each  $R^e$  is optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_n$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, and optionally substituted  $-(CR^a_2)_n$ heterocycloalkyl;

15       $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted  $-C_1-C_4$  alkyl,  $-OR^b$ , oxo, cyano,  $-CF_3$ , optionally substituted phenyl, and  $-C(O)OR^h$ ;

20      Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

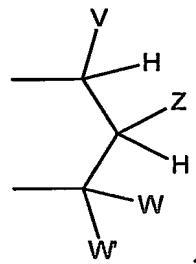
25       $R^5$  is selected from the group consisting of  $-OH$ , optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ ,  $-F$ ,  $-NHC(O)R^e$ ,  $-NHS(=O)_2R^e$ ,  $-NHS(=O)R^e$ ,  $-NHC(=S)NH(R^h)$ , and  $-NHC(O)NH(R^h)$ ;

30       $R^7$  is selected from the group consisting of hydrogen, halogen, amino, hydroxyl,  $-O-C_1-C_4$  alkyl,  $-SH$  and  $-S-C_1-C_4$  alkyl;

X is  $P(O)YR^{11}Y'R^{11}$ ;

Y and Y' are each independently selected from the group consisting of  $-O-$ , and  $-NR^v-$ ; when Y and Y' are  $-O-$ , R<sup>11</sup> attached to  $-O-$  is independently selected from the group consisting of H, alkyl, optionally substituted aryl, optionally substituted

- heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  
 $-C(R^z)_2OC(O)NR^{z_2}$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  
 $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
5 and -alkyl-S-S-alkylhydroxy;  
when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H,  $[C(R^z)_2]_q-COOR^y$ ,  $C(R^x)_2COOR^y$ ,  $[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;
- 10 when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^{z_2}$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  
 $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
15 and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H,  $[C(R^z)_2]_q-COOR^y$ ,  $C(R^x)_2COOR^y$ ,  $[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;  
or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together  
20 R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



wherein:

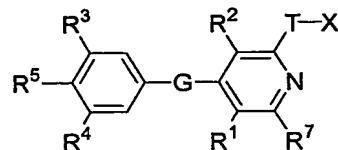
- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- 5        or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;
- 10      or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;
- 15      or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- 20      or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0–2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- 25      Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;
- 25      q is an integer 2 or 3;
- 30      Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;
- 30      Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;
- 30      Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;
- 30      Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;
- 30      with the provisos that:

- a) when G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -C(O)- and -NR<sup>b</sup>-, T is -A-B- where A is selected from the group consisting of  
5 -NR<sup>b</sup>-, -O-, -CH<sub>2</sub>- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl; R<sup>3</sup> is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or  
10 unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, and substituted or unsubstituted C<sub>3</sub>-C<sub>5</sub> cycloalkyl; R<sup>7</sup> is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl; and R<sup>5</sup> is selected from the group consisting of hydroxyl, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, and -OC(O)R<sup>e</sup>; then X is not -P(O)(OH)<sub>2</sub>;
- b) V, Z, W, W' are not all -H; and
- c) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;
- 20 and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.
200. The method of claim 198 wherein when G is -O-, T is -NH-CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each chloro, R<sup>3</sup> is *iso*-propyl, R<sup>7</sup> is fluoro, and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.
201. The method of claim 199 wherein when G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -C(O)- and -NR<sup>b</sup>-, T is -A-B- where A is selected from the group consisting of -NR<sup>b</sup>-, -O-, -CH<sub>2</sub>- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl; R<sup>3</sup> is selected from the group consisting of halogen, trifluoromethyl, substituted or  
30 unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R<sup>4</sup> is selected from the group consisting of hydrogen, halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, and substituted or

unsubstituted heteroaryl; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, substituted or unsubstituted C<sub>3</sub>-C<sub>5</sub> cycloalkyl; and R<sup>7</sup> is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl; then R<sup>5</sup> is  
5 not hydroxyl, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, or -OC(O)R<sup>e</sup>.

202. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

- 10      G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;
- T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
15     -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>;
- k is an integer from 0-4;
- m is an integer from 0-3;
- n is an integer from 0-2;
- 20     p is an integer from 0-1;
- Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso  
25     that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;
- Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, 5 optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;

R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally 10 substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>cycloalkyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;

15 Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;

20 Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;

25 R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup> and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected 30 from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl,

optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and  
optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

$R^5$  is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>,

5 -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);

$R^7$  is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl;

X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;

Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>- OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

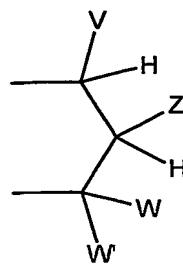
when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,

25 -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>- OC(O)R<sup>y</sup>,

-C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,

and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

30 or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, 5 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
    - or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,
  - 10 alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
    - or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the
  - 15 phosphorus;
    - or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that
  - 20 is three atoms from a Y attached to the phosphorus;
    - or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
  - 25 or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,

-SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
 -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

5 Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

10 Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

15 Each R<sup>y</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

a) when G is -O-, T is -NH-CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each chloro, R<sup>3</sup> is iso-propyl, R<sup>4</sup> is hydrogen, R<sup>7</sup> is fluoro and R<sup>5</sup> is -OH, then X is not P(O)(OH)<sub>2</sub>,

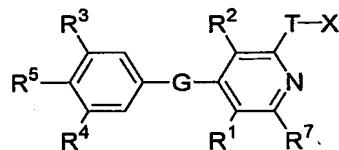
15 P(O)(OH)(OCH<sub>3</sub>) or P(O)(OCH<sub>3</sub>)<sub>2</sub>;

b) V, Z, W, W' are not all -H; and

c) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

203. The method of claim 100 wherein said phosphonic acid-containing compound is a compound of Formula III:



wherein:

25 G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,

$-(CR^a_2)_nCH(NR^bR^c)-$ ,  $-C(O)(CR^a_2)_m-$ ,  $-(CR^a_2)_mC(O)-$ ,  $-(CR^a_2)C(O)(CR^a_2)_n-$ ,  
 $-(CR^a_2)_nC(O)(CR^a_2)-$ , and  $-C(O)NH(CR^b_2)(CR^a_2)_p-$ ;

k is an integer from 0-4;

m is an integer from 0-3;

5 n is an integer from 0-2;

p is an integer from 0-1;

Each  $R^a$  is independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_4$  alkyl, halogen,  $-OH$ , optionally substituted  $-O-C_1-C_4$  alkyl,  $-OCF_3$ , optionally substituted  $-S-C_1-C_4$  alkyl,  $-NR^bR^c$ , optionally substituted  $-C_2-C_4$  alkenyl, and optionally substituted  $-C_2-C_4$  alkynyl; with the proviso that when one  $R^a$  is attached to C through an O, S, or N atom, then the other  $R^a$  attached to the same C is a hydrogen, or attached via a carbon atom;

Each  $R^b$  is independently selected from the group consisting of hydrogen and optionally substituted  $-C_1-C_4$  alkyl;

15 Each  $R^c$  is independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_4$  alkyl, optionally substituted  $-C(O)-C_1-C_4$  alkyl, and  $-C(O)H$ ;

$R^1$  and  $R^2$  are each independently selected from the group consisting of halogen, optionally substituted  $-C_1-C_4$  alkyl, optionally substituted  $-S-C_1-C_3$  alkyl, optionally substituted  $-C_2-C_4$  alkenyl, optionally substituted  $-C_2-C_4$  alkynyl,  $-CF_3$ ,  $-OCF_3$ , optionally substituted  $-O-C_1-C_3$  alkyl, and cyano;

$R^3$  and  $R^4$  are each independently selected from the group consisting of hydrogen, halogen,  $-CF_3$ ,  $-OCF_3$ , cyano, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_m$  aryl, optionally substituted  $-(CR^a_2)_m$  cycloalkyl, optionally substituted  $(CR^a_2)_m$  heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-S(=O)_2NR^fR^g$ ,  $-C(O)NR^fR^g$ ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)_2R^e$ ,  $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;

20 Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$  aryl, optionally substituted  $-(CR^b_2)_n$  cycloalkyl, optionally substituted  $-(CR^b_2)_n$  heterocycloalkyl, and  $-C(O)NR^fR^g$ ;

25 Each  $R^e$  is optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_n$  aryl,  $-490-$

optionally substituted  $-(CR^a_2)_n$ cycloalkyl, and optionally substituted  $-(CR^a_2)_n$ heterocycloalkyl;

- $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted  $-C_1-C_4$  alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

Each R<sup>h</sup> is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

- $R^5$  is selected from the group consisting of -OH, optionally substituted  $-OC_1-C_6$  alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);

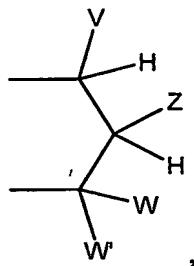
$R^7$  is selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl;

X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;

- Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;
- when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

when Y is -O- and Y' is NR<sup>y</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally

- 5 substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>- OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>y</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;
- 10 or when Y and Y' are independently selected from -O- and -NR<sup>y</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



wherein:

- 15 V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- 20 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0 – 1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- 25 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0–1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that  
5 is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

or together W and W' are connected via an additional 2-5 atoms to form a cyclic  
10 group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>,  
-CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,  
-SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
15 -R<sup>z</sup>, -NR<sup>z</sup>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
-(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;  
q is an integer 2 or 3;

Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and  
20 aralkyl;

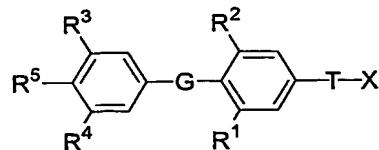
Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl,  
alkoxycarbonyloxyalkyl, and lower acyl;

25 with the provisos that:

a) when G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-,  
-CH<sub>2</sub>, C(O) and -NR<sup>b</sup>; T is -A-B- where A is selected from the group consisting of -  
NR<sup>b</sup>-, -O-, -CH<sub>2</sub>- and -S- and B is selected from the group consisting of a bond and  
substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl; R<sup>3</sup> is selected from the group consisting of  
30 halogen, trifluoromethyl, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or  
unsubstituted aryl, substituted or unsubstituted heteroaryl, aryloxy, substituted amide,  
sulfone, sulfonamide and C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl  
ring(s) are attached or fused to the aromatic; R<sup>4</sup> is selected from the group consisting of  
hydrogen, halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted

- aryl, and substituted or unsubstituted heteroaryl; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, and substituted or unsubstituted C<sub>3</sub>-C<sub>5</sub> cycloalkyl; R<sup>7</sup> is selected selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub>
- 5 alkyl; and R<sup>5</sup> is selected from the group consisting of hydroxyl, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, and -OC(O)R<sup>e</sup>; then X is not -P(O)(OH)<sub>2</sub>;
- c) V, Z, W, W' are not all -H; and
- d) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;
- 10 and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.
204. The method of claim 202 wherein when G is -O-, T is -NH-CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each chloro, R<sup>3</sup> is *iso*-propyl, R<sup>7</sup> is fluoro and R<sup>5</sup> is -OH, then R<sup>4</sup> is not hydrogen.
205. The method of claim 203 wherein when G is selected from the group
- 15 consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -C(O)- and -NR<sup>b</sup>-; T is -A-B- where A is selected from the group consisting of -NR<sup>b</sup>-, -O-, -CH<sub>2</sub>- and -S- and B is selected from the group consisting of a bond and substituted or unsubstituted C<sub>1</sub>-C<sub>3</sub> alkyl; R<sup>3</sup> is selected from the group consisting of halogen, trifluoromethyl, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, substituted or unsubstituted
- 20 heteroaryl, aryloxy, substituted amide, sulfone, sulfonamide and C<sub>3</sub>-C<sub>7</sub> cycloalkyl, wherein said aryl, heteroaryl or cycloalkyl ring(s) are attached or fused to the aromatic; R<sup>4</sup> is selected from the group consisting of is hydrogen, halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>6</sub> alkyl, substituted or unsubstituted aryl, and substituted or unsubstituted heteroaryl; R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group
- 25 consisting of halogen, substituted or unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, and substituted or unsubstituted C<sub>3</sub>-C<sub>5</sub> cycloalkyl; and R<sup>7</sup> is selected selected from the group consisting of hydrogen, halogen, amino, hydroxyl, -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl; then R<sup>5</sup> is not hydroxyl, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, or -OC(O)R<sup>e</sup>.
- 30 206. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of Formula I:



wherein:

- G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;
- 5        T is selected from the group consisting of -(CR<sup>a</sup>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup>)<sub>n</sub>-, -(CR<sup>a</sup>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup>)<sub>2</sub>-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup>)<sub>2</sub>-, -O(CR<sup>b</sup>)<sub>2</sub>(CR<sup>a</sup>)<sub>n</sub>-, -S(CR<sup>b</sup>)<sub>2</sub>(CR<sup>a</sup>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup>)<sub>2</sub>(CR<sup>a</sup>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup>)<sub>n</sub>-, -(CR<sup>a</sup>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup>)<sub>m</sub>-, -(CR<sup>a</sup>)<sub>m</sub>C(O)-, -(CR<sup>a</sup>)C(O)(CR<sup>a</sup>)<sub>n</sub>-, -(CR<sup>a</sup>)<sub>n</sub>C(O)(CR<sup>a</sup>)<sub>p</sub>-, and -C(O)NH(CR<sup>b</sup>)<sub>2</sub>(CR<sup>a</sup>)<sub>p</sub>;
- 10      k is an integer from 0-4;
- m is an integer from 0-3;
- n is an integer from 0-2;
- p is an integer from 0-1;
- Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;
- 15      Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;
- Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;
- 20      R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;
- 25      R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally
- 30      halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally

substituted  $-(CR^a_2)_m$ aryl, optionally substituted  $-(CR^a_2)_m$ cycloalkyl, optionally substituted  $-(CR^a_2)_m$ heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-S(=O)_2NR^fR^g$ ,  $-C(O)NR^fR^g$ ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)_2R^e$ ,  $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;

5        Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, and  $-C(O)NR^fR^g$ ;

10      Each  $R^e$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_n$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, and optionally substituted  $-(CR^a_2)_n$ heterocycloalkyl;

15       $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected 20 from the group consisting of optionally substituted  $-C_1-C_4$  alkyl,  $-OR^b$ , oxo, cyano,  $-CF_3$ , optionally substituted phenyl, and  $-C(O)OR^h$ ;

25      Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

30       $R^5$  is selected from the group consisting of  $-OH$ , optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ ,  $-F$ ,  $-NHC(O)R^e$ ,  $-NHS(=O)R^e$ ,  $-NHS(=O)_2R^e$ ,  $-NHC(=S)NH(R^h)$ , and  $-NHC(O)NH(R^h)$ ;

35      X is  $P(O)YR^{11}Y'R^{11}$ ;

40      Y and Y' are each independently selected from the group consisting of  $-O-$ , and  $-NR^v-$ ; when Y and Y' are  $-O-$ , R<sup>11</sup> attached to  $-O-$  is independently selected from the group consisting of H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,

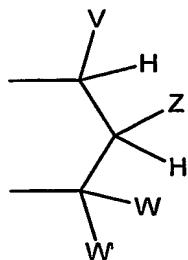
-C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>,  
 -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
 and -alkyl-S-S-alkylhydroxy;

when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected

- 5 from the group consisting  
 of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>,  
 and -cycloalkylene-COOR<sup>y</sup>;

- when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected  
 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted  
 10 heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety  
 contains a carbonate or thiocarbonate, optionally  
 substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>,  
 -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy,  
 and -alkyl-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from  
 15 the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>,  
 and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together  
 R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the  
 group:



20

wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen,  
 optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,  
 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and  
 25 optionally substituted 1-alkynyl;

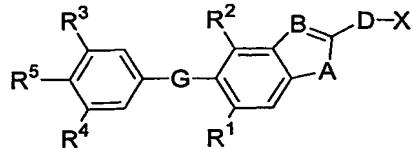
or together V and Z are connected via an additional 3-5 atoms to form a cyclic  
 group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining  
 atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

- alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;
- or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;
- or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>, -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH, -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl, -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;
- q is an integer 2 or 3;
- Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;
- Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;
- Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;
- Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;
- with the provisos that:
- V, Z, W, W' are not all -H; and
  - when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs

and a pharmaceutically acceptable carrier.

207. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of Formula II:



wherein:

A is selected from the group consisting of -NR<sup>i</sup>-, -O-, and -S-;

B is selected from the group consisting of -CR<sup>b</sup>-, and -N-;

10 R<sup>i</sup> is selected from the group consisting of hydrogen, -C(O)C<sub>1</sub>-C<sub>4</sub> alkyl, -C<sub>1</sub>-C<sub>4</sub> alkyl, and -C<sub>1</sub>-C<sub>4</sub>-aryl;

R<sup>b</sup> is selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -CH<sub>2</sub>-, -CF<sub>2</sub>-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

D is selected from the group consisting of a bond, -(CR<sup>a</sup>)<sub>2</sub>-, and -C(O)-;

Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;

20 R<sup>1</sup> and R<sup>2</sup> are each independently selected from the group consisting of halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano;

25 R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>cycloalkyl, optionally

30 substituted -(CR<sup>a</sup>)<sub>m</sub>arylp, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>cycloalkyl, optionally substituted -(CR<sup>a</sup>)<sub>m</sub>cycloalkenyl, and optionally substituted -(CR<sup>a</sup>)<sub>m</sub>cycloalkynyl;

substituted  $-(CR^a_2)_m$ heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-S(=O)_2NR^fR^g$ ,  $-C(O)NR^fR^g$ ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)_2R^e$ ,  $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;

Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, and  $-C(O)NR^fR^g$ ;

Each  $R^e$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_n$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, and optionally substituted  $-(CR^a_2)_n$ heterocycloalkyl;

$R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted  $-C_1-C_4$  alkyl,  $-OR^b$ , oxo, cyano,  $-CF_3$ , optionally substituted phenyl, and  $-C(O)OR^h$ ;

Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

$R^5$  is selected from the group consisting of -OH, optionally substituted  $-OC_1-C_6$  alkyl,  $-OC(O)R^e$ ,  $-OC(O)OR^h$ ,  $-F$ ,  $-NHC(O)R^e$ ,  $-NHS(=O)R^e$ ,  $-NHS(=O)_2R^e$ ,  $-NHC(=S)NH(R^h)$ , and  $-NHC(O)NH(R^h)$ ;

X is  $P(O)YR^{11}Y'R^{11}$ ;

Y and Y' are each independently selected from the group consisting of -O-, and  $-NR^V$ ; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,

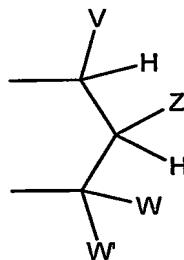
$-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are  $-NR^v-$ , then R<sup>11</sup> attached to  $-NR^v-$  is independently selected from the group consisting

- 5 of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>,

when Y is  $-O-$  and Y' is  $NR^v$ , then R<sup>11</sup> attached to  $-O-$  is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted  $CH_2$ -heterocycloalkyl wherein the cyclic moiety 10 contains a carbonate or thiocarbonate, optionally substituted -alkylaryl,  $-C(R^z)_2OC(O)NR^z_2$ ,  $-NR^z-C(O)-R^y$ ,  $-C(R^z)_2-OC(O)R^y$ ,  $-C(R^z)_2-O-C(O)OR^y$ ,  $-C(R^z)_2OC(O)SR^y$ , -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to  $-NR^v-$  is independently selected from the group consisting of -H,  $-[C(R^z)_2]_q-COOR^y$ ,  $-C(R^x)_2COOR^y$ ,  $-[C(R^z)_2]_q-C(O)SR^y$ , and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from  $-O-$  and  $-NR^v-$ , then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



- 20 wherein:

V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;

- 25 or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is

- 5 fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;

or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy,

- 10 alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;

or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

- 15 or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>,  
 -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OCO<sub>2</sub>R<sup>y</sup>, -OR<sup>z</sup>,  
 20 -SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
 -R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
 -(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

- 25 Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

- 30 Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxy carbonyloxyalkyl, and lower acyl;

with the provisos that:

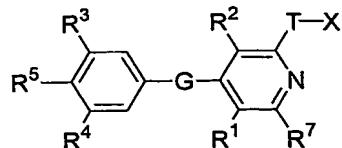
a) V, Z, W, W' are not all -H; and

b) when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically acceptable salts of said prodrugs.

and a pharmaceutically acceptable carrier.

208. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound of Formula III:



wherein:

G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)₂-, -CH₂-, -CF₂-, -CHF-, -C(O)-, -CH(OH)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;

10 T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>-,

15 k is an integer from 0-4;

m is an integer from 0-3;

n is an integer from 0-2;

p is an integer from 0-1;

Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, 20 optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;

25 Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;

Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;

$R^1$  and  $R^2$  are each independently selected from the group consisting of halogen, optionally substituted  $-C_1-C_4$  alkyl, optionally substituted  $-S-C_1-C_3$  alkyl, optionally substituted  $-C_2-C_4$  alkenyl, optionally substituted  $-C_2-C_4$  alkynyl,  $-CF_3$ ,  $-OCF_3$ , optionally substituted  $-O-C_1-C_3$  alkyl, and cyano;

- 5        $R^3$  and  $R^4$  are each independently selected from the group consisting of hydrogen, halogen,  $-CF_3$ ,  $-OCF_3$ , cyano, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_m$ aryl, optionally substituted  $-(CR^a_2)_m$ cycloalkyl, optionally substituted  $-(CR^a_2)_m$ heterocycloalkyl,  $-OR^d$ ,  $-SR^d$ ,  $-S(=O)R^e$ ,  $-S(=O)_2R^e$ ,  $-S(=O)_2NR^fR^g$ ,  
10       $-C(O)NR^fR^g$ ,  $-C(O)OR^h$ ,  $-C(O)R^e$ ,  $-N(R^b)C(O)R^e$ ,  $-N(R^b)C(O)NR^fR^g$ ,  $-N(R^b)S(=O)_2R^e$ ,  
           $-N(R^b)S(=O)_2NR^fR^g$ , and  $-NR^fR^g$ ;

Each  $R^d$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, and  $-C(O)NR^fR^g$ ;

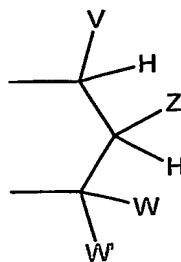
15      Each  $R^e$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^a_2)_n$ aryl, optionally substituted  $-(CR^a_2)_n$ cycloalkyl, and optionally substituted  $-(CR^a_2)_n$ heterocycloalkyl;

20       $R^f$  and  $R^g$  are each independently selected from the group consisting of hydrogen, optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl, or  $R^f$  and  $R^g$  may together form an optionally substituted heterocyclic ring, which may contain a second heterogroup selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally substituted  $-C_1-C_4$  alkyl,  $-OR^b$ , oxo, cyano,  $-CF_3$ , optionally substituted phenyl, and  $-C(O)OR^h$ ;

25      Each  $R^h$  is selected from the group consisting of optionally substituted  $-C_1-C_{12}$  alkyl, optionally substituted  $-C_2-C_{12}$  alkenyl, optionally substituted  $-C_2-C_{12}$  alkynyl, optionally substituted  $-(CR^b_2)_n$ aryl, optionally substituted  $-(CR^b_2)_n$ cycloalkyl, and optionally substituted  $-(CR^b_2)_n$ heterocycloalkyl;

$R^5$  is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>b</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>b</sup>), and -NHC(O)NH(R<sup>b</sup>);

- $R^7$  is selected from the group consisting of hydrogen, halogen, amino, hydroxyl,  
 5 -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -SH and -S-C<sub>1</sub>-C<sub>4</sub> alkyl;  
 X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;  
 Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted  
 10 heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;  
 15 when Y and Y' are -NR<sup>v</sup>, then R<sup>11</sup> attached to -NR<sup>v</sup> is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;  
 when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected  
 20 from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloakyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup> is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;  
 25 or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the  
 30 group:



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl,
- 5 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy,
- 10 alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
- or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the phosphorus;
- 15 or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that is three atoms from a Y attached to the phosphorus;
- or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- 20 or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of -CHR<sup>z</sup>OH, -CHR<sup>z</sup>OC(O)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)R<sup>y</sup>, -CHR<sup>z</sup>OC(S)OR<sup>y</sup>, -CHR<sup>z</sup>OC(O)SR<sup>y</sup>, -CHR<sup>z</sup>OC(=O)R<sup>y</sup>, -OR<sup>z</sup>,

-SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
-R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
-(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

5        Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and  
aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or  
together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

10      Each R<sup>y</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl,  
alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

a)      V, Z, W, W' are not all -H; and

b)      when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl,

15      or heterocycloalkyl;

and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically  
acceptable salts of said prodrugs.

and a pharmaceutically acceptable carrier.

209.     The pharmaceutical composition as in any of claims 206, 207, or 208  
20        wherein said pharmaceutical composition is in the form of a controlled release  
composition.

210.     The pharmaceutical composition as in any of claims 206, 207, or 208  
wherein said pharmaceutical composition is in the form of a transdermal patch.

211.     The pharmaceutical composition as in any of claims 206, 207, or 208  
25        wherein said pharmaceutical composition is in the form of a tablet.

212.     The pharmaceutical composition as in any of claims 206, 207, or 208  
wherein said pharmaceutical composition is in the form of a hard capsule.

213.     The pharmaceutical composition as in any of claims 206, 207, or 208  
wherein said pharmaceutical composition is in the form of a soft capsule.

30        214.    The pharmaceutical composition as in any of claims 206, 207, or 208  
wherein said pharmaceutical composition comprises a crystalline form of said compound  
of Formula I, II, or III.

215. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition comprises a salt form of said compound of Formula I, II, or III.

216. The pharmaceutical composition as in any of claims 206, 207, or 208  
5 wherein said pharmaceutical composition is administered orally in a unit dose of about 0.375 µg/kg to 3.375 mg/kg.

217. The pharmaceutical composition of claim 216 wherein said unit dose is about 3.75 µg/kg to 0.375 mg/kg.

218. The pharmaceutical composition of claim 216 wherein said unit dose is  
10 about 3.75 µg/kg to 37.5 µg/kg.

219. The pharmaceutical composition of claim 216 wherein said unit dose is about 3.75 µg/kg to 60 µg/kg.

220. The pharmaceutical composition of claim 216 wherein said unit dose is about 0.188 µg/kg to 1.88 mg/kg.

221. The pharmaceutical composition of claim 216 wherein said unit dose is about 1.88 µg/kg to .188 mg/kg.

222. The pharmaceutical composition of claim 216 wherein said unit dose is about 1.88 µg/kg to 18.8 µg/kg.

223. The pharmaceutical composition of claim 216 wherein said unit dose is  
20 about 1.88 µg/kg to 30 µg/kg.

224. The pharmaceutical composition as in any of claims 206, 207, or 208 wherein said pharmaceutical composition is administered orally in a total daily dose of about 0.375 µg/kg/day to about 3.75 mg/kg/day, equivalent of the free acid.

225. The pharmaceutical composition of claim 224 wherein said total daily  
25 dose is about 3.75 µg/kg/day to about 0.375 mg/kg/day, equivalent of the free acid.

226. The pharmaceutical composition of claim 224 wherein said total daily dose is about 30 µg/kg/day to about 3.0 mg/kg/day, equivalent of the free acid.

227. A phosphonic acid containing thyromimetic compound of Formula X:

30  $(Ar^1)-G-(Ar^2)-T-X$

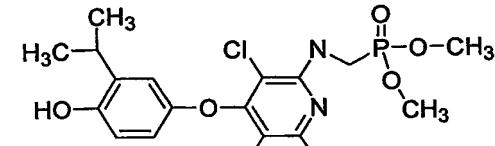
wherein:

$Ar^1$  and  $Ar^2$  are aryl groups;

G is an atom or group of atoms that links Ar<sup>1</sup> and Ar<sup>2</sup> through a single C, S, O, or N atom;

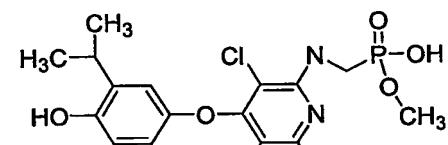
T is an atom or group of atoms linking Ar<sup>2</sup> to X through 1-4 contiguous atoms or is absent;

- 5        X is a -P(O)(OH)<sub>2</sub> or prodrug thereof;  
       wherein (Ar<sup>1</sup>)-G-(Ar<sup>2</sup>)-T-P(O)(OH)<sub>2</sub> has a Ki of ≤ 150 nM relative to T3;  
       with the provisos that said -P(O)(OH)<sub>2</sub> containing thyromimetic compound is  
       not:

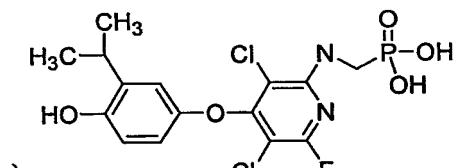


a)

10

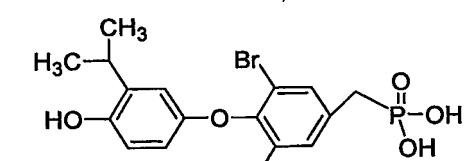


b)

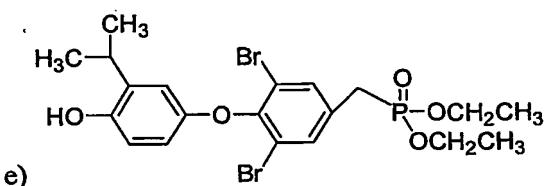


c)

15

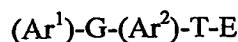


d)



e)

228. A method of improving liver versus heart selectivity of a thyromimetic compound of Formula Y:



5

wherein:

$Ar^1$  and  $Ar^2$  are aryl groups;

G is an atom or group of atoms that links  $Ar^1$  and  $Ar^2$  through a single C, S, O, or N atom;

10 T is an atom or group of atoms linking  $Ar^2$  to E through 1-4 contiguous atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a  $pK_a \leq 7.4$ , a carboxylic acid moiety or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TR $\alpha$  or TR $\beta$ , comprising the step of  
15 replacing E with a  $-P(O)(OH)_2$  or prodrug thereof.

229. A method of increasing the therapeutic index of a thyromimetic compound of Formula Y:



wherein:

$Ar^1$  and  $Ar^2$  are aryl groups;

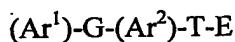
G is an atom or group of atoms that links  $Ar^1$  and  $Ar^2$  through a single C, S, O, or  
25 N atom;

T is an atom or group of atoms linking  $Ar^2$  to E through 1-4 atoms or is absent;

E is selected from the group consisting of a functional group or moiety with a  $pK_a \leq 7.4$ , a carboxylic acid moiety or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TR $\alpha$  or TR $\beta$ , comprising the step of  
30 replacing E with a  $-P(O)(OH)_2$  or prodrug thereof.

230. A method of designing a thyromimetic compound with improved liver versus heart selectivity comprising the steps of:

obtaining a molecular formula for a thyromimetic of Formula Y:



wherein:

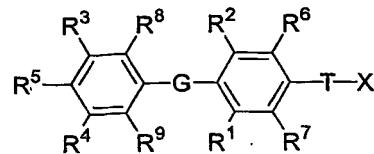
- 5         $Ar^1$  and  $Ar^2$  are aryl groups;  
G is an atom or group of atoms that links  $Ar^1$  and  $Ar^2$  through a single C, S, O, or N atom;  
T is an atom or group of atoms linking  $Ar^2$  to E through 1-4 contiguous atoms or is absent;
- 10      E is selected from the group consisting of a functional group or moiety with a  $pK_a \leq 7.4$ , a carboxylic acid moiety, or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TR $\alpha$  or TR $\beta$ ; comprising the step of replacing E with a  $-P(O)(OH)_2$  or prodrug thereof; and synthesizing a compound of Formula X wherein X is  $-P(O)(OH)_2$  acid or prodrug thereof.
- 15      231. A method of designing a thyromimetic compound with an improved therapeutic index comprising the steps of:  
obtaining a molecular formula for a thyromimetic of Formula Y:



wherein:

- Ar<sup>1</sup> and Ar<sup>2</sup> are aryl groups;  
G is an atom or group of atoms that links Ar<sup>1</sup> and Ar<sup>2</sup> through a single C, S, O, or N atom;  
T is an atom or group of atoms linking Ar<sup>2</sup> to E through 1-4 atoms or is absent;  
E is selected from the group consisting of a functional group or moiety with a  $pK_a \leq 7.4$ , a carboxylic acid moiety, or an atom or group of atoms containing an O or N that binds the thyroid hormone binding pocket of a TR $\alpha$  or TR $\beta$ ; comprising the step of replacing E with a  $-P(O)(OH)_2$  or prodrug thereof; and synthesizing a compound of Formula X wherein X is  $-P(O)(OH)_2$  acid or prodrug thereof.

## 232. A compound of Formula VIII:



wherein:

- G is selected from the group consisting of -O-, -S-, -S(=O)-, -S(=O)<sub>2</sub>-, -Se-,  
5 -CH<sub>2</sub>-,-CF<sub>2</sub>-,-CHF-, -C(O)-, -CH(OH)-, -CH(C<sub>1</sub>-C<sub>4</sub> alkyl)-, -CH(C<sub>1</sub>-C<sub>4</sub> alkoxy)-,  
-C(=CH<sub>2</sub>)-, -NH-, and -N(C<sub>1</sub>-C<sub>4</sub> alkyl)-;
- T is selected from the group consisting of -(CR<sup>a</sup><sub>2</sub>)<sub>k</sub>-, -CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-CR<sup>b</sup>=CR<sup>b</sup>-, -(CR<sup>a</sup><sub>2</sub>)-CR<sup>b</sup>=CR<sup>b</sup>-(CR<sup>a</sup><sub>2</sub>)-, -O(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
-S(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>c</sup>)(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-, -N(R<sup>b</sup>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
10 -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>CH(NR<sup>b</sup>R<sup>c</sup>)-, -C(O)(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>-, -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>C(O)-, -(CR<sup>a</sup><sub>2</sub>)C(O)(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>-,  
-(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>C(O)(CR<sup>a</sup><sub>2</sub>)-, and -C(O)NH(CR<sup>b</sup><sub>2</sub>)(CR<sup>a</sup><sub>2</sub>)<sub>p</sub>;
- k is an integer from 0-4;
- m is an integer from 0-3;
- n is an integer from 0-2;
- 15 p is an integer from 0-1;
- Each R<sup>a</sup> is independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, halogen, -OH, optionally substituted -O-C<sub>1</sub>-C<sub>4</sub> alkyl, -OCF<sub>3</sub>, optionally substituted -S-C<sub>1</sub>-C<sub>4</sub> alkyl, -NR<sup>b</sup>R<sup>c</sup>, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, and optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl; with the proviso  
20 that when one R<sup>a</sup> is attached to C through an O, S, or N atom, then the other R<sup>a</sup> attached to the same C is a hydrogen, or attached via a carbon atom;
- Each R<sup>b</sup> is independently selected from the group consisting of hydrogen and optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl;
- Each R<sup>c</sup> is independently selected from the group consisting of hydrogen and  
25 optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -C(O)-C<sub>1</sub>-C<sub>4</sub> alkyl, and -C(O)H;
- R<sup>1</sup>, R<sup>2</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, and R<sup>9</sup> are each independently selected from the group consisting of hydrogen, halogen, optionally substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, optionally substituted -S-C<sub>1</sub>-C<sub>3</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>4</sub> alkenyl, optionally

substituted -C<sub>2</sub>-C<sub>4</sub> alkynyl, -CF<sub>3</sub>, -OCF<sub>3</sub>, optionally substituted-O-C<sub>1</sub>-C<sub>3</sub> alkyl, and cyano; with the proviso that at least one of R<sup>1</sup> and R<sup>2</sup> is not hydrogen;

or R<sup>6</sup> and T are taken together along with the carbons they are attached to form a ring of 5 to 6 atoms including 0 to 2 heteroatoms independently selected from -NR<sup>i</sup>-, -O-, and -S-, with the proviso that when there are 2 heteroatoms in the ring and both heteroatoms are different than nitrogen then both heteroatoms have to be separated by at least one carbon atom; and X is attached to this ring by a direct bond to a ring carbon, or by -(CR<sup>a</sup><sub>2</sub>)- or -C(O)- bonded to a ring carbon or a ring nitrogen;

R<sup>i</sup> is selected from the group consisting of hydrogen, -C(O)C<sub>1</sub>-C<sub>4</sub> alkyl,  
10 -C<sub>1</sub>-C<sub>4</sub> alkyl, and -C<sub>1</sub>-C<sub>4</sub>-aryl;

R<sup>3</sup> and R<sup>4</sup> are each independently selected from the group consisting of hydrogen, halogen, -CF<sub>3</sub>, -OCF<sub>3</sub>, cyano, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>cycloalkyl, optionally 15 substituted -(CR<sup>a</sup><sub>2</sub>)<sub>m</sub>heterocycloalkyl, -OR<sup>d</sup>, -SR<sup>d</sup>, -S(=O)R<sup>e</sup>, -S(=O)<sub>2</sub>R<sup>e</sup>, -S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, -C(O)NR<sup>f</sup>R<sup>g</sup>, -C(O)OR<sup>h</sup>, -C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)R<sup>e</sup>, -N(R<sup>b</sup>)C(O)NR<sup>f</sup>R<sup>g</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>R<sup>e</sup>, -N(R<sup>b</sup>)S(=O)<sub>2</sub>NR<sup>f</sup>R<sup>g</sup>, and -NR<sup>f</sup>R<sup>g</sup>;

Each R<sup>d</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl,  
20 optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, and -C(O)NR<sup>f</sup>R<sup>g</sup>;

Each R<sup>e</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and  
25 optionally substituted -(CR<sup>a</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl;

R<sup>f</sup> and R<sup>g</sup> are each independently selected from the group consisting of hydrogen, optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup><sub>2</sub>)<sub>n</sub>heterocycloalkyl, or R<sup>f</sup>  
30 and R<sup>g</sup> may together form an optionally substituted heterocyclic ring, said heterocyclic ring may contain a second heterogroup within the ring selected from the group consisting of O, NR<sup>c</sup>, and S, wherein said optionally substituted heterocyclic ring may be substituted with 0-4 substituents selected from the group consisting of optionally

substituted -C<sub>1</sub>-C<sub>4</sub> alkyl, -OR<sup>b</sup>, oxo, cyano, -CF<sub>3</sub>, optionally substituted phenyl, and -C(O)OR<sup>h</sup>;

Each R<sup>h</sup> is selected from the group consisting of optionally substituted -C<sub>1</sub>-C<sub>12</sub> alkyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkenyl, optionally substituted -C<sub>2</sub>-C<sub>12</sub> alkynyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>aryl, optionally substituted -(CR<sup>b</sup>)<sub>n</sub>cycloalkyl, and optionally substituted -(CR<sup>b</sup>)<sub>n</sub>heterocycloalkyl;

R<sup>5</sup> is selected from the group consisting of -OH, optionally substituted -OC<sub>1</sub>-C<sub>6</sub> alkyl, -OC(O)R<sup>e</sup>, -OC(O)OR<sup>h</sup>, -F, -NHC(O)R<sup>e</sup>, -NHS(=O)R<sup>e</sup>, -NHS(=O)<sub>2</sub>R<sup>e</sup>, -NHC(=S)NH(R<sup>h</sup>), and -NHC(O)NH(R<sup>h</sup>);

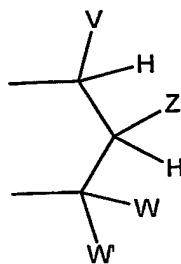
10 X is P(O)YR<sup>11</sup>Y'R<sup>11</sup>;

Y and Y' are each independently selected from the group consisting of -O-, and -NR<sup>v</sup>-; when Y and Y' are -O-, R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy;

when Y and Y' are -NR<sup>v</sup>-, then R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

when Y is -O- and Y' is NR<sup>v</sup>, then R<sup>11</sup> attached to -O- is independently selected from the group consisting of -H, alkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted CH<sub>2</sub>-heterocycloalkyl wherein the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted -alkylaryl, -C(R<sup>z</sup>)<sub>2</sub>OC(O)NR<sup>z</sup><sub>2</sub>, -NR<sup>z</sup>-C(O)-R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-OC(O)R<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>-O-C(O)OR<sup>y</sup>, -C(R<sup>z</sup>)<sub>2</sub>OC(O)SR<sup>y</sup>, -alkyl-S-C(O)R<sup>y</sup>, -alkyl-S-S-alkylhydroxy, and -alkyl-S-S-S-alkylhydroxy; and R<sup>11</sup> attached to -NR<sup>v</sup>- is independently selected from the group consisting of -H, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-COOR<sup>y</sup>, -C(R<sup>x</sup>)<sub>2</sub>COOR<sup>y</sup>, -[C(R<sup>z</sup>)<sub>2</sub>]<sub>q</sub>-C(O)SR<sup>y</sup>, and -cycloalkylene-COOR<sup>y</sup>;

or when Y and Y' are independently selected from -O- and -NR<sup>v</sup>-, then together R<sup>11</sup> and R<sup>11</sup> are -alkyl-S-S-alkyl- to form a cyclic group, or together R<sup>11</sup> and R<sup>11</sup> are the group:



wherein:

- V, W, and W' are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted aralkyl, heterocycloalkyl, aryl, 5 substituted aryl, heteroaryl, substituted heteroaryl, optionally substituted 1-alkenyl, and optionally substituted 1-alkynyl;
    - or together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 atoms, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, substituted with hydroxy, acyloxy, alkylthiocarbonyloxy, 10 alkoxy carbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or
      - or together V and Z are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, that is fused to an aryl group at the beta and gamma position to the Y attached to the 15 phosphorus;
    - or together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxy carbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said carbon atoms that 20 is three atoms from a Y attached to the phosphorus;
  - or together Z and W are connected via an additional 3-5 atoms to form a cyclic group, wherein 0-1 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
    - or together W and W' are connected via an additional 2-5 atoms to form a cyclic group, wherein 0-2 atoms are heteroatoms and the remaining atoms are carbon, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;
- Z is selected from the group consisting of - $\text{CHR}^z\text{OH}$ , - $\text{CHR}^z\text{OC(O)R}^y$ , - $\text{CHR}^z\text{OC(S)R}^y$ , - $\text{CHR}^z\text{OC(S)OR}^y$ , - $\text{CHR}^z\text{OC(O)SR}^y$ , - $\text{CHR}^z\text{OC(O)CO}_2\text{R}^y$ , - $\text{OR}^z$ ,

-SR<sup>z</sup>, -CHR<sup>z</sup>N<sub>3</sub>, -CH<sub>2</sub>aryl, -CH(aryl)OH, -CH(CH=CR<sup>z</sup>)OH, -CH(C≡CR<sup>z</sup>)OH,  
-R<sup>z</sup>, -NR<sup>z</sup><sub>2</sub>, -OCOR<sup>y</sup>, -OCO<sub>2</sub>R<sup>y</sup>, -SCOR<sup>y</sup>, -SCO<sub>2</sub>R<sup>y</sup>, -NHCOR<sup>z</sup>, -NHCO<sub>2</sub>R<sup>y</sup>, -CH<sub>2</sub>NHaryl,  
-(CH<sub>2</sub>)<sub>q</sub>-OR<sup>z</sup>, and -(CH<sub>2</sub>)<sub>q</sub>-SR<sup>z</sup>;

q is an integer 2 or 3;

5        Each R<sup>z</sup> is selected from the group consisting of R<sup>y</sup> and -H;

Each R<sup>y</sup> is selected from the group consisting of alkyl, aryl, heterocycloalkyl, and  
aralkyl;

Each R<sup>x</sup> is independently selected from the group consisting of -H, and alkyl, or  
together R<sup>x</sup> and R<sup>x</sup> form a cyclic alkyl group;

10      Each R<sup>v</sup> is selected from the group consisting of -H, lower alkyl, acyloxyalkyl,  
alkoxycarbonyloxyalkyl, and lower acyl;

with the provisos that:

a)      when G is -O-, T is -CH<sub>2</sub>-, R<sup>1</sup> and R<sup>2</sup> are each bromo, R<sup>3</sup> is *iso*-propyl, R<sup>4</sup>  
is hydrogen, and R<sup>5</sup> is -OH, then X is not P(O)(OH)<sub>2</sub> or P(O)(OCH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>;

15      b)      V, Z, W, W' are not all -H; and

c)      when Z is -R<sup>z</sup>, then at least one of V, W, and W' is not -H, alkyl, aralkyl,  
or heterocycloalkyl;

d)      when G is -O-, T is -(CH<sub>2</sub>)<sub>0-4</sub>-, R<sup>1</sup> and R<sup>2</sup> are independently halogen,  
alkyl of 1 to 3 carbons, and cycloalkyl of 3 to 5 carbons, R<sup>3</sup> is alkyl of 1 to 4 carbons or  
20     cycloalkyl of 3 to 7 carbons, R<sup>4</sup> is hydrogen, and R<sup>5</sup> is -OH, then X is not -P(O)(OH)<sub>2</sub> or  
-P(O)(O lower alkyl)<sub>2</sub>; and

e)      when G is -O-, R<sup>5</sup> is -NHC(O)R<sup>e</sup>, -NHS(=O)<sub>1-2</sub>R<sup>e</sup>, -NHC(S)NH(R<sup>h</sup>), or  
-NHC(O)NH(R<sup>h</sup>), T is -(CH<sub>2</sub>)<sub>m</sub>-, -CH=CH-, -O(CH<sub>2</sub>)<sub>1-2</sub>-, or -NH(CH<sub>2</sub>)<sub>1-2</sub>-, then X is not  
-P(O)(OH)<sub>2</sub> or -P(O)(OH)NH<sub>2</sub>;

25      and pharmaceutically acceptable salts and prodrugs thereof and pharmaceutically  
acceptable salts of said prodrugs.

233. A method of increasing the liver specificity of a T3 mimetic having a  
carboxylic acid moiety comprising the preparation of a compound that is an analog of  
said T3 mimetic wherein said carboxylic acid moiety is replaced by P(O)(OH)<sub>2</sub> and  
30     prodrugs thereof.

234. A method of selecting a T3 mimetic having enhanced liver specificity  
comprising the steps of:

- a) measuring the liver specificity of a T3 mimetic having a carboxylic acid moiety;
  - b) measuring the liver specificity of a compound that is an analog of said T3 mimetic having a carboxylic acid moiety wherein the carboxylic acid moiety is replaced by a P(O)(OH)<sub>2</sub> or prodrug thereof;
  - 5 c) comparing the liver specificities of steps a) and b).
235. A method of screening T3 mimetics comprising the steps of:
- 10 a) measuring a biological effect of T3 mimetic having a carboxylic acid moiety wherein said biological effect is selected from the group consisting of the Ki relative to T3, effects on blood glucose level, effects on serum cholesterol level, effects on fat in the liver, liver specificity, and therapeutic index;
  - b) measuring the same biological effect measured in a) of a T3 mimetic having a phosphonic acid or prodrug moiety thereof; and
  - 15 c) comparing the results in steps a) and b);
  - d) selecting the T3 mimetic of step b) for further scientific evaluation.

236. A compound as in any of claims 1, 2, 117, 139, 140, or 232, wherein said compound is in the form of a co-crystal.

237. The method of claim 135 wherein said metabolic disease is NASH.

238. The method of claim 135 wherein said metabolic disease is selected from the group consisting of impaired glucose tolerance, diabetes, and metabolic syndrome X.